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All of Us Are Deeply Concerned about the Outcome of Present Efforts in Restoring National Prosperity.—Coöperation Is the First Step toward Progress—Pharmacy Is Strengthened by That Which Makes It of Greater Service.

Vol. XXIII, No. 2 FEBRUARY, 1934

JOURNAL
OF THE
AMERICAN PHARMACEUTICAL ASSOCIATION

TRADE MARK

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THE 82nd ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION WILL BE HELD IN WASHINGTON, D. C., DURING WEEK OF MAY 7, 1934.

The 1934 Meetings of the American Association of Colleges of Pharmacy, the National Association of Boards of Pharmacy, Conference of Pharmaceutical Association Secretaries, of the Pharmaceutical Law Enforcement Officials and the Plant Science Seminar will also be held in Washington.

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PHARMACY AND THE DRUG STORE.

This is no time to criticize, unless the purpose is to be helpful to coöperate in improving conditions that exist, to establish confidence.

A disturbing factor starts most of us to thinking; it is unnecessary to be reminded of how conditions developed that cause us to realize what our standing is and be convinced that we have not been as earnest as we should have in persistently striving to attain the opportunity that is always beckoning to us from the horizon of the future. Fifty years ago, William S. Thompson, of Washington, D. C., then president of the AMERICAN PHARMACEUTICAL ASSOCIATION, said in his presidential address: "Are we not justified in the belief that from the present trade conflict there will survive a higher pharmacy than that of our time? We are sustained in this opinion by a survey of the entire situation of pharmacy in this country. . . . characteristic of our country in all that pertains to science and art—our profession will not lag behind, but the followers fully equipped with knowledge and skill, will stand shoulder to shoulder with the most advanced; and with equal strides will move on to that brighter era for which they appear to be preparing."

The representative of the U. S. Public Health Service at the Diamond Anniversary Meeting of the A. PH. A. said that "the thing which challenged his admiration more than anything else was the evident broadening scope of the organization—the broad statesmanship displayed in the laudable effort to bring together many divergent interests which have, however, one objective in common—the advancement of pharmacy."

The closing paragraph of an editorial in the *Australasian Journal of Pharmacy* seems applicable and is quoted: "The call in pharmacy to-day is the will to adopt a plan and to stick to it until it is brought to a final and successful conclusion. There is much that cannot be done—there are forces that cannot be overcome by direct attack—but by means of flank attacks and concerted action by the whole body along definite lines the way can be paved to brighter and better things. The heritage of pharmacy lies in the traditions of the past. Its future depends on those who are practising its profession to-day. Great responsibility is cast on those who are leading in the van, but equally so is the need on the part of all of the true coöperative spirit that is willing to sacrifice to some extent its individuality in order to gain a greater success for the good of all."

We are not merely passive observers of a stupendous national drama, and our destiny is dependent on our resourcefulness and our character. A result for the good of the public should come out of this adjustment in restricting the sale and dispensing of medicines to those qualified by education and training. Times like the present bring to the fore a realization of conditions which have not heretofore been disturbing factors and it is to be hoped that the public will gain a clearer appreciation of the fundamentally important rôle of pharmacy for its protection.

In proper shaping of affairs the thought must lead that success depends on unison in action as far as this is reasonably possible, and confidence within the groups is essential, strengthened by a right understanding with related activities.

DR. ROBERT P. FISCHELIS.

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

VOL. XXIII FEBRUARY, 1934 No. 2

ROBERT PHILIP FISCHELIS.

Robert P. Fischelis, president-elect of the AMERICAN PHARMACEUTICAL ASSOCIATION, son of Philip and Ernestine (Kempt) Fischelis, was born in Philadelphia, Pa., August 16, 1891. He received his early education in St. Paul's Lutheran Parochial School, Philadelphia, and the public schools of that city, graduating from the Northeast High School in 1908. The same year he engaged with James Huston, prescription pharmacist, Philadelphia. The following year he entered the Pharmacy School of the Medico-Chirurgical College of Philadelphia, graduating at the head of his class in 1911. Among the five medals and prizes he received was a year's membership in the AMERICAN PHARMACEUTICAL ASSOCIATION, offered by Prof. George R. Meeker for the highest mark in analytical chemistry. He immediately joined the ASSOCIATION and has been a member ever since. Dr. Fischelis continued his studies in the Department of Pharmaceutical Chemistry of the Medico-Chirurgical College and in the College of Liberal Arts and Sciences of Temple University, receiving the Ph.C. degree from the former and the B.Sc. in Chemistry from the latter.

In 1912, he began teaching Pharmacy and Organic Chemistry in the Department of Pharmacy of the Medico-Chirurgical College, and also taught Pharmacy in the Department of Medicine. During this period he took up graduate work and, later, received the Doctorate in Pharmacy from the Medico-Chirurgical College. In addition to his education in Pharmacy and Chemistry, Dr. Fischelis also took courses in Bacteriology at the University of Pennsylvania Summer School, and courses in Economics at the Wharton School of Commerce and Finance of the University of Pennsylvania. After the Pharmacy School of the Medico-Chirurgical College merged with the Philadelphia College of Pharmacy and Science, the degree of Master of Pharmacy (in course) was conferred upon him.

In 1914, Dr. Fischelis became associate editor of the *Druggists Circular*, which was then under the editorial guidance of Dr. H. V. Arny. While holding this position he continued teaching on a part-time schedule in Philadelphia. He left

the *Druggists Circular* in 1916 to join the Scientific Staff of the H. K. Mulford Company in Philadelphia, continuing part-time teaching at the Medico-Chirurgical College and, later, at the Philadelphia College of Pharmacy and Science.

He left the Mulford Company to join the Chemical Warfare Service, U. S. A., during the War. Upon leaving the army, he opened his own office in New York City as a consulting pharmacist and chemist. He also joined the editorial staff of *Industrial and Engineering Chemistry* under Dr. C. H. Herty and, later, became managing editor of the *News Edition* of that publication. He relinquished this post in 1928 because of pressure of other duties.

From 1921 to 1925, Dr. Fischelis was dean and professor of Pharmacy at the New Jersey College of Pharmacy in Newark, New Jersey. During his incumbency, this institution grew from a student body of approximately fifty to one of about two hundred and fifty. Official recognition was granted the college during this period in the states of New Jersey and New York, Pennsylvania and others and it also obtained membership in the American Association of Colleges of Pharmacy. He was instrumental in beginning negotiations for the affiliation of the college with Rutgers University and conducted a campaign for funds among its alumni and friends for a new building. He was elected vice-president of the American Association of Colleges of Pharmacy in 1924. He resigned as dean of the New Jersey College of Pharmacy in 1925, spent several months recovering from a breakdown in health and then resumed his consulting practice and continued his editorial activities. At this time he also became educational advisor to the Board of Pharmacy of the state of New Jersey. In 1926, he was offered and accepted the secretaryship of the Board of Pharmacy of the state of New Jersey; upon the demise of the late Prof. Jeannot Hostmann, he was also made chief chemist of the Board, and has held these positions since 1926, making his headquarters in Trenton.

The president-elect has been active in association work for many years. From 1913 to 1915, he was secretary of the Philadelphia Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION. In 1916, he was secretary of the Section on Commercial Interests, A. PH. A., and the following year he served as chairman of this section. From 1923 to 1925, he served as secretary of the Council of the AMERICAN PHARMACEUTICAL ASSOCIATION and chairman of the Committee on Publications. From 1931 to 1933, he was president of the New York Branch, A. PH. A., was elected first vice-president of the parent ASSOCIATION in 1933 and is now serving in that capacity.

Both the Pennsylvania and the New Jersey Pharmaceutical Associations have been served by Dr. Fischelis in an executive capacity. From 1916 to 1919 he was secretary of the Pennsylvania Pharmaceutical Association, and in 1919 he became its president. He founded and edited the *Pennsylvania Pharmacist* while secretary of the Association. In 1926, when the late Professor Hostmann, secretary of the New Jersey Pharmaceutical Association, passed away, Dr. Fischelis was asked to accept the secretaryship for the unexpired term and was persuaded to continue in that office until 1929, when he resigned because of pressure of his official duties and new work undertaken for the Committee on the Costs of Medical Care. While secretary of the New Jersey Pharmaceutical Association, he founded and edited the *New Jersey Journal of Pharmacy*. He also served this Association as second vice-president in 1923–1924 and as first vice-president in 1924–1925. At present he is a member of the Board of Trustees of the Association and chairman of several

of its committees. Since 1931, he has been vice-president and chairman of District No. 2 of the National Association of Boards of Pharmacy. From 1920 to 1932 he was editor of the news service of the Drug Trade Bureau of Public Information. He has edited the Charter's Report, published under the title "Basic Material for a Pharmaceutical Curriculum."

Dr. Fischelis is a member of the American Chemical Society, the American Public Health Association, the American Medical Association, the Chemists' Club of New York, the Rotary Club of Trenton and a fellow of the American Association for the Advancement of Science. He was a delegate to the U. S. P. Revision Conventions of 1920 and 1930, and is a member of the A. PH. A. Recipe Book Committee.

He is a member of the Kappa Psi fraternity, the Beta Phi Sigma, Phi Lambda Upsilon, honorary Chemical Society, and a member of the American Legion. He is a former president of the Alumni Association, Department of Pharmacy, Medico-Chirurgical College and of the Alumni Association of the Philadelphia College of Pharmacy and Science.

Since 1926, he has been a coöperating state official of the U. S. Food and Drug Administration, and he has also taken an active part in the Conference of Pharmaceutical Law Enforcement Officials. He gives an annual series of lectures on pharmaceutical journalism and on patents and trade-marks at The Philadelphia College of Pharmacy and Science.

As a member of the Research Staff of the Committee on the Costs of Medical Care, Dr. Fischelis, in coöperation with Dr. C. Rufus Rorem, made a survey of the manufacture and distribution of drugs and medicines in the United States and the services of pharmacy in medical care. The results of this survey have been published by the University of Chicago Press in book form under the title "The Costs of Medicines." He is a frequent contributor to various pharmaceutical and chemical publications, and is the author of the chapter entitled "Medical Materials Industry" found in Volume X of the Encyclopedia of the Social Sciences. Section III of the National Pharmaceutical Syllabus, dealing with State Board examinations, was written by Dr. Fischelis, who was also chairman of the sub-committee on cultural and basic subjects of the Syllabus Committee.

In 1933, he was appointed a member of the Governor's School Survey Commission which has been engaged in studying the educational program of the state of New Jersey.

In 1919, Dr. Fischelis married Miss Juanita C. Deer of Chicago.

Hygiene Exposition Held in Lima.—The President of the Republic inaugurated on December 10th for 15 days the First International Hygiene Exposition held in this city under the auspices of the Bureau of Health, Ministry of Fomento. (Commercial Attache Julian D. Smith, Lima.)

Druggists' Exhibit at the Leipzig Sample Fall Fair 1933 Proves Great Attraction.—The official figures of the Leipzig sample fall fair of 1933 included also the exhibitors at the "Brown Fair" held on the Fair Grounds, where the Association of Leipzig Druggists maintained a collective exhibition for advertising and propaganda purposes. While this special exhibit of Leipzig druggists proved a great attraction for the local visitors and those from neighboring cities, its effect on the wholesale and export business was slight. (Vice-Consul P. Mallon, Leipzig.)

EDITORIAL

E. G. EBERLE, EDITOR 2215 Constitution Ave., WASHINGTON, D. C.

THE PHARMACY EXHIBIT—A CENTURY OF PROGRESS INTERNATIONAL EXPOSITION.

THE 1933 Pharmacy Exhibit of the World's Fair will very likely be continued this year; Medicine and Dentistry have decided on doing so. Illustrations of the Pharmacy Exhibit are shown in the January (1933) number of the JOURNAL, pages 1 and 4 and in the July issue, pages 592 and 594, and comments appear in the same numbers and also elsewhere in other issues of the year. The Committee on Pharmacy Exhibit consisting of H. C. Christensen, *Chairman;* J. H. Riemenschneider, *Treasurer*, and Frank B. Kirby, *Secretary*, has issued a general letter to the press acknowledging contributions and thanking the contributors and co-operators for their financial help and valuable services, including manufacturers and wholesalers, associations, publications, retailers and individuals.

The following is quoted from the letter of appreciation in which the names of the donors are given:

"Invaluable aid in planning and building the exhibit material was rendered by sub-committees, the chairmen of which were as follows: Educational, C. B. Jordan; Historical, Edward Kremers; United States Pharmacopœia, E. Fullerton Cook; Legislation, R. L. Swain; Service in Public Health, E. F. Kelly; Professional, C. Leonard O'Connell.

"Special mention for valuable assistance in installation work, personnel, etc., is also due to R. W. Terry and E. N. Gathercoal, of the University of Illinois; Edward Ireland, of the University of Wisconsin; H. W. Heine and C. J. Zufall, of Purdue University; also O. U. Sisson of Chicago.

"The Committee is indebted to the pharmaceutical press of the country for the splendid publicity given to the exhibit; to the Century of Progress officials for the donation of the space, including electricity, this being the biggest debt, as the space had a commerical value of approximately $15,000; to Mrs. Lillian H. Bowen for handling the correspondence and clerical details of the exhibit; to Thaddeus Niemic, who had charge of the professional demonstrations; and to Miss Esther H. Barney, Superintendent of the Exhibit, goes a large share of the credit for the day to day success of the exhibit in impressing the thousands of visitors, both professional and laymen, with the importance of pharmacy and pharmaceutical service in the field of public health."

We would repeat what was said in a number of the issues of the JOURNAL regarding the exhibit and express appreciation for the outstanding work of the committee; American pharmacy is indebted to the members for the services rendered by them. Acknowledgment was made by resolution at the meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION in Madison, and further expressions of appreciation by individuals, affiliated bodies and other organizations evidenced the importance of the exhibit.

While the value of the Exhibit is recognized as a pronounced success the committee feels that a number of improvements can be made and invites suggestions for carrying on the exhibit this year. Further comments will be made in succeeding numbers of the JOURNAL with the purpose of giving the members of the committee every possible assistance. Pharmacy was given equal recognition with related professions in the Medical Section. The exhibit provided a valuable contact with the public and a publicity which greatly benefits pharmacy.

PAN-AMERICAN MEDICAL ASSOCIATION.

LAST year pharmacists were invited to participate in the program of the pharmacopœial section of the Pan-American Medical Association meeting in Dallas. Theodore J. Bradley presided over the sessions, at which time many papers bearing on pharmacopœial work were read and the possibilities of "Pan-American Pharmacopœial Uniformity" were presented in a paper by E. Fullerton Cook, printed in the May JOURNAL for 1933, page 456.

Pharmacists are again invited to participate in the program. In the paper referred to it was pointed out that "the establishment of a Section on Pharmacopœias as a regular function of the organization opens a new line of interest and service in Pan-American coöperation which is most gratifying. The idea of a Pan-American Pharmacopœia and in fact the effort to develop an 'International Pharmacopœia' is not new, but every earlier effort failed because such an idea is not in conformity with the spirit of strong nationalism which exists in every country. We may well benefit from the experience of the international groups who made their first progress by agreeing upon a policy which did not interfere with the continuance of their own national Pharmacopœia but, in principle, obtained practically all of the benefits of an 'International Pharmacopœia.'"

This year's conference will be held on the S. S. Pennsylvania. A program has been outlined for the floating Congress to Venezuela, March 14th–30th.

Many of the papers will be read during a four-day session at sea, but there will be a session in Venezuela also. The physicians will visit Colon, Cartagena, Puerto Cabello, Caracas, La Guayra and San Juan, P. R. In Venezuela the members of the party will be entertained at Maracay, the home of President Gomez. The party will then go to Caracas; returning by way of San Juan the members will be guests of the Governor of Puerto Rico, Dr. Morales Otero, president of the Medical Association in Puerto Rico, and Dr. George Bachman, director of the School of Tropical Medicine, Columbia University of Puerto Rico.

HISTORICAL PHARMACIES.

THE following resolution was adopted at the Madison meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION:

Resolved, that the Local Branches of the AMERICAN PHARMACEUTICAL ASSOCIATION, State Pharmaceutical Associations, Boards and Colleges of Pharmacy as well as other organizations and individuals interested in the progress and development of pharmacy be urged to supply documents of historical interest, relics and museum material to the museum and library of the Headquarters Building of the AMERICAN PHARMACEUTICAL ASSOCIATION at Washington and be it further

Resolved, that organizations and individuals interested in the progress of pharmacy be urged to prepare papers on matters of historical interest for presentation to the Section on Historical Pharmacy of the AMERICAN PHARMACEUTICAL ASSOCIATION.

The purpose of this comment is to bring to the attention of pharmacists the possibilities of preserving historical pharmacies in various localities. This was brought to mind by a brief history of Apothecaries Hall, New Haven, Conn., published in connection with the celebration of the 150th anniversary of the New

Haven County Medical Society (1934) and the 113th anniversary of Apothecaries Hall. The history of the latter was prepared by the son of Emil A. Gessner,[1] long a member of the AMERICAN PHARMACEUTICAL ASSOCIATION and, until his demise, February 3, 1930, proprietor of Apothecaries Hall.

A replica of Philo Carpenter's drug store, Chicago, is part of the Pharmacy Exhibit—A Century of Progress—a sketch by William B. Day is printed in the September JOURNAL for 1931, pages 922–924. A sketch of General Mercer and his apothecary shop appears in the June number of the JOURNAL for 1926, page 425. The list of pharmacies which have been depicted can be extended, but the purpose is to awaken an interest to preserve historical pharmacies or place plates on the buildings that housed them, which will acquaint the citizens and visitors with related historical data.

Recently, the Leadbeater Pharmacy has been purchased for the AMERICAN PHARMACEUTICAL ASSOCIATION. It is the intention of the Association for the Preservation of Alexandria Antiquities to restore the interior and open the building as a museum. During a recent visit the doors that belonged to the pharmacy in its earliest days were found in the attic. Its restoration will make it possible to visit where Washington had his medicines prepared by Edward Stabler, the founder of "Leadbeater Pharmacy."

The Headquarters Building is now prepared to receive historical material for its museum—an historical description should accompany the contribution.

CENSUS OF THE DRUG INDUSTRY AND PHARMACY.

THE Bureau of Census for the calendar year 1933 is in preparation and the Department is urging all activities to reply promptly in giving the information requested in the circular. The importance for doing so is in the fact that the data will be helpful in presenting conditions in the industry on which action may be taken on questions that concern druggists and pharmacists. Without such information misunderstandings are bound to occur, without the possibility of presenting necessary details. Arguments in attempting to arrive at conclusions regarding the code have shown that officials are not always informed on questions applying to the drug store that are very different from those in other activities.

No similar census has been undertaken since 1929 and the Bureau is asking that druggists render complete reports promptly. When the reports have been received separate compilations are to be made covering the different divisions of the drug industry. This comment is prompted by the belief that this census is of greater importance than those immediately preceding.

Cod Liver Oil Steaming Plants in Norway.—There are approximately 800 steaming plants in Norway, according to an estimate furnished by the Bureau of Fisheries. The total number of producers of raw cod liver oil is unknown, but exporters estimate the total to be around 500 who produce from 2 to 20 barrels each. The number of such producers has been decreasing from year to year as fast as new steaming plants have been opened in the various districts. (Office of the Consulate, Bergen.)

[1] See November JOURNAL, 1928, page 1071.

SCIENTIFIC SECTION

BOARD OF REVIEW OF PAPERS.—*Chairman*, L. W. Rowe, George D. Beal, F. F. Berg, C. O. Lee, E. V. Lynn, John C. Krantz, Jr., Heber W. Youngken.

ANTIDOTES. III. THALLIUM.*

BY JAMES C. MUNCH, CONSULTING PHARMACOLOGIST, BUREAU OF BIOLOGICAL SURVEY, GLENOLDEN, PA.

In 1924 laboratory investigations suggested the value of thallium in the control of various rodents. Field tests conducted in the next few years validated our laboratory conclusions (19, 21). Literature did not reveal any definite information regarding antidotes for thallium poisoning, so studies along this line were undertaken. These experiments were conducted in the Washington laboratory of the Bureau of Chemistry (now called the Food and Drug Administration) of the United States Department of Agriculture at an elevation of about one hundred feet above sea-level. Thallium sulphate solutions were included in the diet, or injected subcutaneously or intravenously into dogs. Less extensive studies were made on rabbits, rats, guinea-pigs and cats. Dogs used in this work were fed 100 Gm. of ground lean meat containing five per cent of dried whole milk powder daily. Bones were included in the diet once a week. Drinking water was available at all times. No evidence of dietary disease was noted among the control animals. The development of thallotoxicosis was followed daily and definite symptoms were recognized as characteristic of thallium poisoning (9, 16, 18, 20). In some experiments the protective procedure was commenced at the time poison was administered. In other experiments treatment was delayed. Chemical studies of thallium elimination under various methods of treatment were contemplated, but were not carried out in detail then because of the lack of suitable analytical methods. With the development of quantitative methods, chemical essays are used to control the efficiency of various procedures.

TABLE I.—CERTAIN LETHAL DOSE OF THALLIUM—MG. TL PER KG.

	Method of Administration.			
Animals.	Oral.	Subcutaneous.	Intraperitoneal.	Intravenous.
Frogs	....	2.5–60 (?)	...	...
		150 (3)		
Birds	35–50	40–160	...	...
Mice	25 (5)	70 (2)	70 (2)	...
			30 (4)	
Rats	25 (5)	60 (2)	60 (1)	
			40 (2)	20–25
Guinea pigs	....	70 (2)	70 (1)	
		10 (5)	10 (5)	25
Rabbits	500	20–60	...	25 (1)
Hedgehogs	....	36	...	...
Cats	250–500	15	...	...
Dogs	15–100	15–45	13	20–25

Foot-note: The figures in parentheses represent the day's interval between injection and death.

The intravenous administration of 25 mg. of thallium per kilo (in the form of thallium sulphate) was followed by death within five to ten days, and this was

* Scientific Section, A. PH. A., Madison meeting, 1933.

selected as the certain lethal dose (L. D. 100). Smaller doses occasionally killed, although the percentage of recoveries increased as the dose decreased. Twenty-five mg. of thallium per kilo fed to rats or intravenously injected in the marginal ear vein of rabbits produced death within three to five days (21). Available results upon toxicity to various animals are given in Table I.

Based on a knowledge of the chemical behavior and toxicity of thallium compounds, various drugs were administered in attempts to counteract the poisonous effects.

(1) *Sodium thiosulphate* had been considered as an antidote in the treatment of heavy metal poisoning, although in 1924 no references to its use in thallotoxicosis were found. Our original tests failed to show definite relief following its use. Oral administration had very little effect. Intravenous injections often increased the severity of thallium symptoms within twenty-four hours. The following year Buschke and Peiser (5, 7, 8) published their study on this question and reached the same conclusion.

(2) The insolubility of the *halides* of thallium led to the study of the possibility of protecting animals by a course of treatment with the chloride or iodide of sodium or potassium. The potassium salts were useful but caused cardiac depression. Administration of sodium chloride was somewhat less effective than sodium iodide. The elimination of thallium was followed by flame tests on twenty-four hour urine samples to determine the relative intensity of green color. Treatment with sodium iodide decreased, and treatment with sodium thiosulphate increased the thallium excretion in the urine.

(3) One outstanding feature of thallium poisoning is the general endocrinological depression. Various endocrine stimulants were considered and finally *pilocarpine* was adopted because of its low toxicity in effective doses. Not only does pilocarpine serve as an endocrine stimulant, but also it stimulates perspiration. As thallium is eliminated in the sweat, this was believed to reduce the strain on the kidneys.

(4) Thallium poisoning produces hypo- or achlorhydria (13, 14, 15, 21). Therefore, *hydrochloric acid* was given by mouth to dogs with some success, as an adjunct to other methods of treatment.

(5) Marked disturbances of *calcium* metabolism have been observed in thallotoxicosis. Our studies did not indicate any particular benefit following the administration of calcium salts alone, but in conjunction with iodide-thiosulphate treatment appeared to favor more rapid recovery.

(6) Subsequent reports of studies on treatment suggested and denied the value of various *glandular extracts*, more particularly thymus, parathyroid and pituitary gland extracts (1, 2, 3, 6, 8, 9, 10, 11, 14, 15, 17, 21, 22, 23, 24). No laboratory studies were made with glandular extracts in the 1924 investigations. The incorporation of various glandular extracts in the treatment of thallium poisoning to dogs in later studies did not appear to be successful.

Based on results obtained in the 1924 animal experiments, it was felt that thallium poisoning would be combated most successfully by: (*a*) intravenous administration of sodium iodide until thallium had practically disappeared from the twenty-four hour urine; (*b*) sodium thiosulphate intravenously to induce gradual elimination of thallium; (*c*) pilocarpine and calcium salts intravenously; and (*d*)

oral administration of hydrochloric acid. This regime based solely upon tests on animals may be inadequate, since there is always a question regarding the efficacy of an antidote *for* humans, unless it is firmly established by experiments *upon* humans. Recognized methods of treating strychnine or arsenic poisoning which were developed upon animals have shown somewhat disappointing results when employed upon man, and vice versa. The need for extreme caution in advocating any specific course of treatment as "a successful antidote" for any poison is appreciated. For this reason this regime was not included in the 1931 report (21) in which reference was made to the use of iodides or chlorides and to sodium thiosulphate intravenously.

What results have been obtained in treating human thallotoxicosis? Thallium is commonly, or at least frequently used in medicine. Of 8006 children who received thallium acetate as a depilatory, 447 were poisoned and 8 died. A number of reports of clinical, cosmetic, rodenticidal and suicidal thallium poisoning have been collected.

The extensive survey by Buschke and Peiser (9) contains several reports of attempts to counteract human thallotoxicosis. Bogdanov and Lasko (4) relieved pains in the extremities in two cases of thallium poisoning by sodium thiosulphate; Mrongowius and Duchan (18) in 1928, and Caluzzi (12) in 1929, observed a decrease in toxicity of thallium salts to older children by administration of 1 to 1.5 Gm. of sodium thiosulphate three times daily. Subsequent administration of sodium thiosulphate accelerated recovery following clinical use of thallium. For the treatment of thallotoxicosis Mrongowius and Duchan (18) recommended a combination of 5 Gm. of sodium thiosulphate and 5 mg. of pilocarpine nitrate in 20 cc. of distilled water. It is of interest, in this connection, that Buschke, Duchan and Joseph (7) were unable to obtain any benefit by using this treatment upon thallium-poisoned animals.

Over thirty-one persons were poisoned by thallium in January 1932, near Fresno, California (16, 20), at an elevation of two hundred feet above sea-level. Fourteen were hospitalized, one being less seriously poisoned than the others. Eight patients who were treated by this regime recovered. Six others who were treated with sodium thiosulphate, dextrose and parathyroid extract died. It is not certain that these eight patients would have died if this regime had not been followed; however, in the opinion of the attending physicians their clinical condition was as serious as the condition of those who died.

CONCLUSIONS.

1. Experiments upon animals in 1924 led to the development of a definite method for combating thallotoxicosis: treatment with sodium iodide, sodium thiosulphate, pilocarpine, calcium salts and hydrochloric acid.

2. This regime was successful in treating eight humans poisoned by thallium; six untreated patients died.

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CERTAIN POISONOUS PLANTS OF WYOMING ACTIVATED BY SELENIUM AND THEIR ASSOCIATION WITH RESPECT TO SOIL TYPES.

BY O. A. BEATH, J. H. DRAIZE, H. F. EPPSON, C. S. GILBERT AND O. C. MCCREARY.

In 1917, the senior author published a brief treatise[1] on the poisonous properties of the two-grooved milk vetch (*Astragalus bisulcatus*). The toxic principles

[1] Wyoming Experiment Station Bulletin 112.

were reported to be soluble in water and not found to be precipitated by basic acetate of lead. Studies and observations made since that time led to the publication of an experiment station bulletin[1] in May 1932, on "Three Poisonous Vetches," by Beath, Draize and Eppson. The authors pointed out that *A. bisulcatus* collected in some areas had an extremely offensive odor, while in other places this feature was lacking entirely. It was further stated that this variation was in a degree due to soil and climatic factors. From the viewpoint of experimental physiological data it was pointed out that at the "past-seeding stage" *A. bisulcatus* plants produced an accumulative type of poisoning accompanied by severe irritation to the gastro-intestinal tract. Members of the chemical research staff then set about to determine the reasons for such behavior in *A. bisulcatus* and other poisonous plants associated with it in habits of growth.

It has now been demonstrated that those *A. bisulcatus* plants yielding a decidedly offensive odor are more toxic than plants of this species lacking in this characteristic. The only variable factor contributing to this difference, so far determined, is the presence of selenium.

With the coöperation of the State Geologist, Dr. S. H. Knight, and his staff, a correlation of some range plants bearing selenium has been made in conjunction with the geological formation upon which the plants grow. Three species of Astragali, *A. bisulcatus*, *A. Grayi* and *A. pectinatus*, *Xylorhiza Parryi*, *Oonopsis condensata*, *Stanleya bipinnata* and *Mentzelia decapetala* represent at this point in our investigations definite indicator plants that have shown the constant presence of selenium when collected on one or more of the following formations: Niobrara, Steele, Pierre, Morrison, Wasatch (as represented by Cooper Basin), Benton, Hilliard-Cody, Lewis, Bridger, and the dark band of the Dakota. These formations are mostly shale. The so-called indicator plants are the richest in selenium when they occur on the undecomposed shale. The element selenium is distributed throughout the entire makeup of these plants. The amount in the above-ground portion of a plant exceeds that found in the root system and quantitatively[2] varies from a trace to a tenth of one per cent selenium (air-dry basis). Poisonous range plants, containing selenium, occurring on the Niobrara, Steele or Pierre shales are more poisonous to live stock, on the average, than the same plants found on the other formations listed above. Whether or not, or to what extent *Stanleya bipinnata*, *Mentzelia decapetala*, *Oonopsis condensata*, *Astragalus pectinatus* and *A. Grayi* are poisonous to live stock when occurring as selenium-free plants has not been determined. *Xylorhiza Parryi* (woody aster) adheres so closely in Wyoming to definite shale zones that the authors have been unable to collect woody aster, selenium-free, in sufficient amounts to conclude feeding trials. Out of twenty-five samples collected in various sections of the state twenty-three were found to contain varying amounts of selenium, depending upon the geological formation from which collections were made. Selenium in woody aster is presumably combined with a toxic saponaceous[3] compound.

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[1] Wyoming Experiment Station Bulletin 189.

[2] Essentially the method of M. Taboury, "Sur la presence accidentelle du selenium dans certains vegetaux," *Compt. rend.*, 195 (1932), 171.

[3] A. J. Ewart, "The Poisonous Action of Ingested Saponins," Council for Scientific and Industrial Research, Melbourne, Australia, 50 (1931), 18.

It is known that *Astragalus bisulcatus* free from selenium is poisonous to live stock, although very much less so, as brought out in this experiment: Forced feeding trials demonstrated that fifty ounces of green *A. bisulcatus* (blooming) selenium-free, per hundredweight of sheep failed to seriously affect an animal, whereas twenty-five ounces per hundredweight of sheep of the same plant, same stage of growth, containing selenium, produced death in a few hours.

The toxic principle or principles of five out of seven of the selenium-bearing range plants (*Astragalus bisulcatus, A. Grayi, A. pectinatus, Oonopsis condensata, Xylorhiza Parryi*) may be extracted freely with water. Similar data for *Stanleya bipinnata* and *Mentzelia decapetala* have not been obtained. This physical aspect introduces a problem of economic significance because it is evident that through the annual decay of the foliage, seeds and roots of these selenium-bearing plants a considerable amount of this element goes back to the soil in a form readily available to any vegetative growth. Water extracts of green *A. bisulcatus* mixed with crude undecomposed Niobrara shale in experimentally controlled plats imparted to barley grown on these plats recognizable amounts of selenium. Barley grown on the same shale composite without the addition of the vetch extract was found not to contain selenium.

Grasses (native) growing in close proximity to type selenium-bearing range plants were found poisonous to guinea pigs when these pigs were allowed to feed on such areas.

Vicia linearis, Thermopsis divaricarpa, Solidago mollis, Melilotus sp., *Iris missouriensis, Juncus balticus* and some native grasses represent a partial list of plants that have been found to contain selenium which were apparently influenced by those plants yielding soluble selenium compounds. This conclusion is based upon the fact that our tests have failed to detect selenium in this same series of plants taken from uncontaminated shales. It is not to be inferred that only the indicator plants listed take up selenium from the original shales. The authors, however, wish to point out the unique selectivity for selenium shown by certain native plants. Among the Astragali closely allied with *A. bisulcatus, A. Grayi* and *A. pectinatus* ecologically may be mentioned *A. carolinianus, A. flexuosus* and *A. Drummondii*, and yet careful tests have failed in detecting the presence of selenium in these last-named vetches.

The following is a partial list of representative plants collected on well-defined shales found to be negative for selenium:

Erigeron microlonchus, Scirpus sp., Glycyrrhiza sp., Sporobolus sp., Glaux maritima, Sarcobatus vermiculatus, Medicago sativa, Artemisia frigida, Arenaria Hookeri, Sium cicutaefolium, Cicuta occidentalis, Delphinium Geyeri, Zygadenus gramineus, Senecio sp., Musineon sp., Oxytropis sp., Chrysothamnus sp., Eurotia lanata, Valeriana sp. and *Plantago sp.*

SELENIUM POISONING.

The fact that a selenium-bearing plant like *Astragalus bisulcatus* has, so far as our studies have gone, given a positive reaction for selenium when collected on either the basal, mid or top zone of a representative shale, *e. g.*, Steele, would sug-

NOTE: *Atriplex Nuttallii* (salt bush) occurring in close proximity to the unaltered Niobrara shales has been found to contain selenium in varying amounts irrespective of other plant associations.

gest that selenium is not restricted to limited areas in these shales. Its original occurrence in such a comparatively few range plants further suggests the firmness with which it must be combined in the soil.

There appear to be several manifestations of selenium poisoning of live stock. Live stock grazing upon selenium-bearing plants may exhibit slightly different types of poisoning, depending upon the species of such plant ingested. Since such variations do occur, it would seem evident that one of two conditions applies. *First*, the various selenium-bearing plants may carry the element in different chemical combinations, or *second*, the selenium may be present in all plants in a similar chemical combination but the presence of other toxic substances may account for variations in the manifestations of poisoning.

In Wyoming the live stock exhibiting this general type of poisoning reveal the following symptoms and lesions at autopsy: The animals, particularly cattle, exhibit early in the stage of poisoning a dullness and a lack of vitality. It is evident early in the stage of poisoning that there is a stasis of the gastro-intestinal tract. There is considerable abdominal pain, with grunting, grating of teeth and salivation. Shortly before the paralytic stage animals exhibit excitement, with a tendency to constantly wander, often aimlessly in circles. The animal may or may not show impairment of vision. Prior to death the animal exhibits varying degrees of paralysis, which becomes serious when it involves the swallowing mechanism. In the cases observed by the authors the immediate cause of death was failure of the respiration.

In general the autopsy findings of animals dying on the range of "Blind Staggers" (the term used locally to denote this type of poisoning) or of the experimental animals dying from the administration of small quantities of the sodium salt of selenious acid are in fair agreement. The parenchymatous organs exhibit varying degrees of congestion, indicating a failing heart and circulation. In cattle the stomachs, particularly the rumen, suggest a rather severe stasis. The entire gastro-intestinal tract exhibits varying degrees of irritation, leading in some cases to hemorrhage. The liver is often severely congested and the gall bladder distended with bile which may or may not exhibit normal color and consistency. The bladder is usually distended with urine. Whether the above conditions are due to lack of smooth muscle tone is not known. Acutely poisoned animals resulting from one exclusive feeding show no marked pathology.

The acute and chronic forms of poisoning mentioned above are responsible for heavy annual live stock losses in Wyoming.

In a recent article in *Science* on "Selenium as an Insecticide"[1] a form of selenium poisoning is reported which would appear to be quite a different form than that noted with the selenium-bearing range plants of Wyoming. The disease referred to in this article is not known to be common in this state, but where cereals, hay, etc., have produced it there is considerable evidence available which indicates that such selenium-carrying feeds were grown upon geological formations which had previously carried a stand of native selenium-bearing plants or had been contaminated by irrigation waters and rains passing over and through soils contaminated by woody aster, vetches, etc.

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[1] E. M. Nelson, A. M. Hurd-Karrer and W. O. Robinson, *Science*, 78 (1933), 124.

THE BIOASSAY OF PICROTOXIN AND COCCULUS INDICUS PREPARATIONS.*

BY JAMES C. MUNCH AND AMELIA M. PONCE.[1]

Cocculus Indicus and its active principle, picrotoxin, have been used for poisoning fish, for increasing the bitter taste of beer, in "knockout drops" and externally against pediculi (17, 19, 24, 25, 27, 28). Pharmacologically, picrotoxin stimulates the medullary centers producing characteristic convulsions, slowing of the pulse (vagal), and an increase in blood pressure, which is followed by paralysis after large doses (1, 24, 25).

Because of the pharmacological and toxicological interest in picrotoxin, this investigation was undertaken with a view of developing a suitable bioassay.

Chemical studies have shown that Cocculus indicus contains between 1.5 and 5.0 per cent of a non-alkaloidal neutral principle, picrotoxin (1, 3, 27). Picrotoxin has been reported to have the formula $C_{30}H_{34}O_{13}$. On dissolving in water it is supposed to split into equal parts of picrotin and picrotoxinin, which are closely related chemically and have similar actions. Picrotoxinin is believed to be somewhat more potent, and some experiments suggest that picrotin, $C_{15}H_{11}O_7$ is inert on cold- and warm-blooded animals (4, 7, 14, 15). The available literature has not given any definite information regarding the relative toxicity of these three products. The data regarding toxicity have been compiled in Table I (1, 2, 3, 4, 5, 6, 8, 9, 12, 13, 14, 18, 20, 23, 26, 27). It is believed that when administered by mouth picrotin is eliminated partly unchanged in the urine, whereas picrotoxinin is decomposed (4). Picrotoxin is soluble in about 8 parts of alcohol or 240 parts of water (19, 25). In our experience some difficulty has been encountered in obtaining this strong a solution and our findings are in agreement with the statement that picrotoxin is slightly soluble in cold water and more soluble in hot water (19).

Chemical and toxicological studies on picrotoxin and its preparations are under way, and will be reported subsequently. This communication deals only with a method of physiological assay which has been developed.

BIOLOGICAL ASSAYS.

(*1*) *Fish.*—The use of picrotoxin as a fish poison suggests the possibility of developing a method for the bioassay of these preparations on fish. However, the data reported in the literature showed so wide a range of effectiveness, and the symptoms reported did not appear to be characteristic, so no quantitative methods have been developed on fish (1, 5, 6, 9, 11, 24).

(*2*) *Crabs.*—*Carcinas maenas*, a European sea crab is reported to be very susceptible, showing convulsions after a dose of 10 *gamma* of picrotoxin. Other crustaceæ are also believed to be susceptible. None of these animals were readily available and have not been studied in this connection. The symptoms reported did not appear to be characteristic of picrotoxin (20, 24, 27, 29).

(*3*) *Frogs.*—Qualitative tests may be conducted with picrotoxin. The injection of 0.5 to 1.0 mg. of picrotoxin to a 30-Gm. *Rana pipiens* produced a characteristic convulsion. Unfortunately cicutoxin produces a similar effect, although somewhat larger doses are required. The front legs are often folded across the breast, the hind legs extended with the web of the foot tightly stretched. A peculiar convulsant shriek is often heard. Death does not ensue for several hours.

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* Scientific Section, A. PH. A., Madison meeting, 1933.

[1] Department of Pharmacology, Sharp and Dohme, Philadelphia, Pa.

The susceptibility of frogs has been found to depend on the temperature, season and species. Frogs may be suitable for qualitative testing but did not appear useful for quantitative bioassays of picrotoxin and its preparations (1, 9, 10, 16, 24, 27).

(4) *Mice.*—In connection with studies on the potency of soporifics, Wieland and Pulewka found that the injection of 2.4 mg. of picrotoxin subcutaneously to male white mice was withstood, but that larger doses caused convulsions. They injected 4 mg. of picrotoxin per Kg. twenty minutes after the injection of the soporific or hypnotic studied (30). Rassers (22) found that picrotoxin subcutaneously injected into mice produced an S-curve response of the tail similar to that produced by morphine. Our studies on the toxicity of picrotoxin subcutaneously injected into the mice were in reasonable agreement among themselves, but the absolute lethal dose varied from day to day. We have, therefore, studied various factors believed to affect these results.

Although much of this work has been done with freshly prepared solutions, which were usually made to contain 1 mg. of picrotoxin per cc. in recently distilled water, solutions several months old have not been found to show any different toxicity. It would appear, therefore, that aqueous solutions are stable for several months.

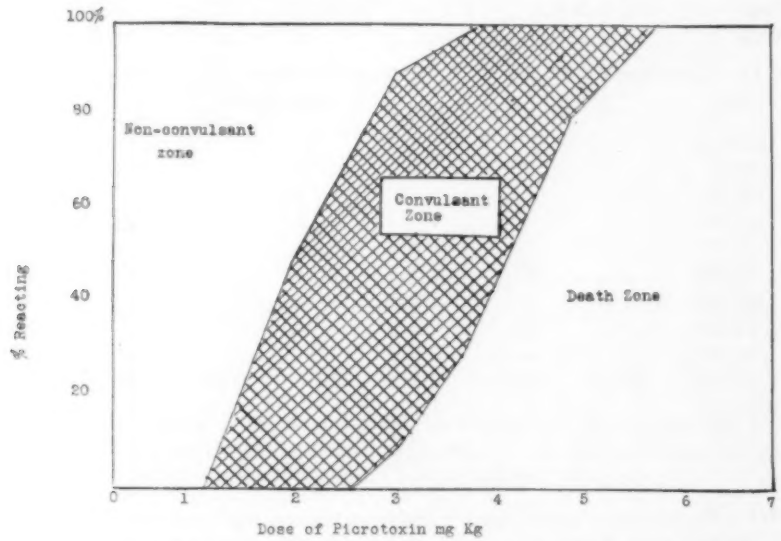

Fig. 1.—Effect of subcutaneous injections of Picrotoxin on mice.

To avoid individual differences in mice, several hundred animals were purchased at a time from different breeders. Mice were weighed to 0.5 Gm. and a measured volume of solution injected under the skin of the abdomen. Care was taken to prevent any loss of solution. The animals were placed in cages and kept under observation for several hours to note the appearance of symptoms. Very soon after injection the animals become quiet. Following this, convulsions develop which are very similar to, but readily differentiated from, those produced by strychnine. No consistent relationship was found between the interval until the development of convulsions, the period until death, and the dose administered. Many mice convulse, but recover. The tail may show various types of curvature, but does not give the characteristic S-curve of morphine.

In a preliminary assay, doses of 4, 5, 6 and 7 mg. of picrotoxin per kilo, and doses of 8 to 14 cc. per kilo of 1:20 dilution of fluidextract (or similar dilutions of other galenicals) are injected subcutaneously into groups of five mice each. The number of convulsions and of deaths are determined over a period of several hours. Under certain conditions, convulsions and deaths have developed within one hour: under other conditions three or four hours may be required. It is difficult to specify a specific time interval, although it appears that one hour would be advisable. Because of the peculiar variations in test animals, both the convulsant and killing doses are considered in reaching a preliminary conclusion. A desirable end-point is the production of convulsions or deaths in sixty to eighty per cent of the injected animals (Fig. 1).

Based upon the results of this preliminary assay, subsequent trials are made injecting groups of five mice each, in an effort to determine the dose of picrotoxin and of the unknown product which produce death in approximately eighty per cent of the injected mice within one hour ($_5LD_{80\%}$). The activity of the unknown product is then estimated in terms of picrotoxin.

The results obtained in testing several samples of tincture and fluidextract of fishberries are given in Tables II and III.

TABLE I.—TOXICITY OF PICROTOXIN AND PICROTOXININ.

Animal.	Subcutaneous.		Intramuscular.		Oral.	
	Picrotoxin.	Picrotoxinin.	Picrotoxin.	Picrotoxinin.	Picrotoxin.	Picrotoxinin.
Rana esculenta	...	1.1–2	2–10	...	...	...
Doves	...	...	1.4	1.6	...	...
Mice	2.5–6	1.6–2.0	...	...	...	...
Guinea pigs	0.3–0.8	...	...	...	...	...
Rabbits	1.3–2.8	1.35–1.6	...	...	2.5	...
Cats	2.0	...	...	...	3.5	...
Dogs	1.5–2.2	1.1	1.0	...	...	...
Man	...	...	...	...	1.0–1.5	...

TABLE II.—CONVULSANT ACTION OF PICROTOXIN ON MICE—SUBCUTANEOUS INJECTIONS.

Date.	Dose, Mg./Kg.				
	1.0 to 1.5.	2.0.	2.5.	3.0.	3.5 to 10.0.
12/27/32	0/3	1/1		1/1	5/5
1/9/33					2/2
1/16/33					1/1
1/17/33				2/2	4/4
1/18/33					1/1
1/20/33		1/1		1/1	1/1
1/24/33		0/2		1/2	4/4
1/27/33		0/2		1/2	8/8
1/30/33		2/2		2/2	2/2
1/31/33		1/1		2/2	1/1
2/1/33		0/1		1/1	2/2
2/5/33		0/1		1/1	1/1
2/6/33		0/2		2/2	3/3
		0/1		1/1	2/2
2/14/33		1/1		1/1	2/2
2/15/33		0/1		1/1	2/2
2/17/33		1/1		1/1	2/2
2/20/33		1/1		1/1	1/1
2/21/33		1/1		1/1	1/1
2/23/33		1/1		1/1	2/2
2/24/33					1/1
2/27/33		1/1		1/1	2/2
3/1/33		1/1		1/1	7/7
3/3/33	0/5		8/10	23/23	76/76
Total	0/8	12/22	8/10	46/48	133/133

This method appears promising for quantitative bioassays of picrotoxin and fishberries preparations.

(*5*) *Rats.*—A similar procedure was used in giving subcutaneous injections of picrotoxin and fishberries solution to white rats weighing between fifty and three hundred and fifty Gm., although most of the test animals weighed about one hundred and fifty Gm. The convulsant and lethal responses were much more erratic than those obtained in using mice. Results obtained with picrotoxin injected into rats are shown in Table IV.

Because of the variability of response, rats did not appear suitable for the bioassay of these products.

TABLE III.—THE TOXICITY OF PICROTOXIN TO MICE—SUBCUTANEOUS INJECTIONS.

Date.	Dose, Mg./Kg.							
	1 to 2.5.	3.0.	3.5.	4.0.	4.5.	5.0.	5.5.	6.0 to 10.
12/27/32	0/6	0/1		0/2		1/2		
1/9/33						1/2		
1/16/33						1/1		
1/17/33		0/2		0/1		2/3		
1/18/33						1/1		
1/20/33	0/1	0/1				1/1		
1/24/33		0/2				1/1		1/1
1/27/33	0/2	0/2		0/2		0/2		2/2
1/30/33	0/2	0/2				1/1		1/1
1/31/33	0/1	0/2				0/1		
2/1/33	0/1	0/1				1/1		1/1
2/5/33	0/1	0/1				1/1		
2/6/33	0/2	0/2				1/2		1/1
2/7/33	0/1	0/1				0/1		1/1
2/10/33	0/1	0/1				1/1		1/1
2/14/33	0/1	0/1				1/1		1/1
2/15/33	0/1	0/1				1/1		1/1
2/20/33	0/1	0/1				1/1		
2/21/33	0/1	0/1				1/1		
2/23/33	0/1	0/1				1/1		1/1
2/24/33						1/1		
2/27/33	0/1	0/1				1/1		1/1
3/3/33	0/1	0/1				1/1		1/1
3/6/33	0/15	16/21	5/23	6/15	7/30	4/4	6/6	5/6
8/7/33				4/10		5/10		
8/10/33				0/5		3/5		
Total	0/40	16/46	5/23	10/35	7/30	33/48	6/6	18/19

(6) *Man.*—It is stated that picrotoxin has been added to beer on account of its bitter taste, and the threshold concentration reported to be bitter is 1:80,000, corresponding to 12.5 mg. per liter (1, 21). The results obtained in testing various concentrations are given in Table V.

TABLE VI.—THRESHOLD LIMEN FOR PICROTOXIN TASTE TESTS.

Concentration, Mg./L.	Bitterness. Subject.					Remarks.
	1.	2.	3.	4.	5.	
5	0	0	0	0	0	
8	0	0	−	+	−	
10	0	0	0	++	0	Slightly astringent
12	0	0	−	−	−	Astringent
15	0	0	−	−	−	
20	0	0	−	−	−	
40	±	±	−	−	−	
50	+	+	−	−	−	
100	++	++	−	−	−	

In our tests on five subjects, one believed the product was definitely "bitter," whereas the other four obtained a taste which was characterized as "astringent." A peculiar numbing of the tongue develops, with various aberrations of sweet and salt tastes. The taste does not appear sufficiently characteristic to justify the use of this method for bioassay.

DISCUSSION.

As a result of our literature studies and of our laboratory tests, we have developed the following bioassay on mice:

TABLE IV.—TOXICITY OF FISHBERRY PREPARATIONS TO MICE.

Sample No.	Product.	Test.	Dose Injected as 10% Tincture Cc./Kg. 2.0.	2.4.	3.0.	4.0.	5.0.	6.0.	7.0.	8.0.	Picrotoxin Mg./Kg. 4.0.	4.5.	5.0.	6.0.	Conclusion.	Mg. Picrotoxin per Cc.
1	F.E.	1			0/2	0/3	0/2	1/4	1/2	4/4		5/10		10/10	0.8 cc. = 6 mg.	7.5
2	F.E.	1			1/5	3/5	7/10	4/5	4/5	4/5	1/2		1/2	1/1		
	F.E.	2				2/5	3/5				2/5		3/5		0.5 cc. = 5 mg.	10.0
3	F.E.	1			0/2	0/2	1/2	2/2			0/2		0/2	1/2		
	F.E.	2				1/5	5/10	8/10			4/10		6/10	5/5		
	F.E.	3				3/5	4/5				2/5		4/5		0.5 cc. = 5 mg.	10.0
4	33% Tr.	1														
	33% Tr.	2	0/5		5/5						2/5		4/5			
	33% Tr.	3	0/5	0/5							2/5		3/5			
											0/5		3/5		1 cc. more than 5 mg.	5.5
															0.8 cc. less than 5 mg.	
5	10% Tr.	1	0/5		0/5	2/5	3/5				0/5		3/5		5 cc. Tr. = 5 mg.	1.0

TABLE V.—THE TOXICITY OF PICROTOXIN TO RATS—SUBCUTANEOUS INJECTION.

Date.	Dose Mg./Kg. 1–2.	3.	4.	5.	6.	7–10.
12/27/32	0/4	1/2	2/2	2/2		4/4
4/17/33		0/5	0/5	2/5	2/3	
4/17/33			2/4	5/5		
		2/5	3/5			
Total	0/4	3/12	7/16	9/12	2/3	4/4

A large number of mice are stored under identical conditions for a sufficient time to insure uniformity. Groups of five mice each are weighed to 0.5 Gm. and injected subcutaneously under the skin of the abdomen with solutions of picrotoxin and of the unknown fishberry product. Typical picrotoxin convulsions and/or death should develop within one hour.

In a preliminary trial, doses of 4, 5, 6 and 7 mg. of picrotoxin per kilo may be administered, and quantities of the fishberry product estimated to be equivalent in picrotoxin content. Subsequent assays should be made, based on the results of this preliminary trial, to determine the amounts of picrotoxin and of the unknown product simultaneously injected which produce death in about eighty per cent of the injected mice. As a suggested standard, 5 mg. of picrotoxin is recommended.

CONCLUSIONS.

1. Great variations in the response of individual animals have been observed following the administration of picrotoxin and of its galenical preparations.

2. By the simultaneous injection of standard picrotoxin and of a galenical subcutaneously to mice, a feasible bioassay has been developed.

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NATIONAL STANDARDS FOR TINCTURE DIGITALIS* WITH SPECIAL REFERENCE TO U. S. P. X AND B. P. 1932 STANDARDS.[1]

BY L. W. ROWE.

A few years ago (1) experimental data were submitted showing the relation among five of the better known methods of bioassay of digitalis and the various standards proposed for these methods. At that time the powdered digitalis leaf standard of the Geneva Conference had not been available long enough to permit of more than a very few comparative tests and it was only then being seriously considered by various foreign countries as a national standard for digitalis assay. Since then Canada, in the Food and Drugs Act Regulations of 1928, and England, in the 1932 revision of the British Pharmacopœia, have definitely made the international powdered digitalis leaves their standard for the bioassay of digitalis. Meanwhile Ouabain has continued as the U. S. Pharmacopœia standard for digitalis and in spite of its being illogical from the standpoint of relative degree of absorption in the short time period (one hour), as previously pointed out, the majority opinion favors its retention in the U. S. P. XI. Very recently Defandorf (2) has advocated revision of the present U. S. P. "One-Hour Frog Method" to permit of a longer time period for more complete absorption and action of the diluted digitalis preparation which would be a valuable step forward. He failed, however, to observe that a difference in degree of absorption between Ouabain and digitalis in any given time and particularly in different frogs may also influence the accuracy of the assay method.

The assay methods which are official in the present U. S. P. and B. P. are sufficiently different to make a comparison of the official tinctures quite difficult and added to this, the marked difference between the standards, Ouabain and International Standard Digitalis Leaves, makes a series of experimental tests the only basis of comparison. This short paper presents such data accumulated since 1930 and permits a conclusion based on averages which should be approximately correct. It should be stated before the assay results are tabulated that both the official B. P. 1932 tincture of digitalis and the standard extract of the international powdered digitalis leaves are made without defatting the drug while the U. S. P. X tincture is made from defatted drug. For some unknown reason the assay results

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* Scientific Section, A. PH. A., Madison meeting, 1933.

[1] From the Research Laboratories of Parke, Davis & Company, Detroit, Michigan.

are more definite and in general the drug is found to be somewhat more active when not defatted, though tests have failed to show any appreciable activity in the fats after removal. It is to be hoped that the U. S. P. XI will not require the drug to be defatted, as it has been clearly shown that the nausea frequently caused by active digitalis preparations is of central origin, and also the presence of the fats does not contribute to the instability of the tincture with any degree of uniformity.

The details of the methods of assay used in this series are available in the U. S. P. X and the B. P. 1932. The Ouabain standard was the official No. 626 obtained from the Food and Drug Administration in Washington. The Canadian Standard digitalis leaves No. 428 was obtained from Ottawa and certified that 0.85 Gm. is equivalent to 1.0 Gm. of International Standard digitalis leaves. This correction was always made in preparing the standard extract. The lot of International Standard used in this series was labeled "Standard Digitalis 1928" and was obtained from the National Institute for Medical Research, London, N. W. 3.

SUMMARY OF ASSAYS.

Sample: International Standard Digitalis.

Method.	Date.	M. L. D. or M. S. D.	Relative Potency.
Lethal Frog	Sept. 1932	0.0075 cc. at 0.0075 cc.	100% of Canad. Std.
Lethal Frog	Jan. 1933	0.0040 cc. at 0.0055 cc.	137.5% of Canad. Std.
4-Hr. Frog	Nov. 1931	0.0060 cc. at 0.0050 cc.	83% of Canad. Std.
4-Hr. Frog	Feb. 1932	0.0040 cc. at 0.0045 cc.	112% of Canad. Std.
4-Hr. Frog	Apr. 1932	0.0040 cc. at 0.0045 cc.	112% of Canad. Std.
4-Hr. Frog	Dec. 1932	0.0060 cc. at 0.0060 cc.	100% of Canad. Std.
M. S. D. Frog	Mar. 1929	0.0080 cc. at 0.0000006 Gm.	110% of U. S. P. Std.
M. S. D. Frog	Oct. 1931	0.0050 cc. at 0.0000005 Gm.	120% of U. S. P. Std.
M. S. D. Frog	Oct. 1932	0.0060 cc. at 0.00000070 Gm.	140% of U. S. P. Std.
M. S. D. Frog	Jan. 1933	0.0060 cc. at 0.00000070 Gm.	140% of U. S. P. Std.
M. S. D. Frog	July 1933	0.0070 cc. at 0.00000060 Gm.	103% of U. S. P. Std.
Cat Method	1929	Av. M. L. D. 1.05 cc./Kg.	95% Hatcher Std.
Cat Method	1933	Av. M. L. D. 1.19 cc./Kg.	86% Hatcher Std.
		Sample: Ouabain U. S. P.	
Cat Method	1929	Av. M. L. D. 0.105 mg./Kg.	95% Hatcher Std.
		Sample: 1932 Digitalis.	
Lethal Frog	Oct. 1932	0.007 cc. at 0.00000033 Gm.	160% for Ouabain U. S. P.
M. S. D. Frog	Oct. 1932	0.006 cc. at 0.00000070 Gm.	140% of U. S. P. Std.
M. S. D. Frog	Oct. 1932	0.006 cc. at 0.006 (Inter. Std.)	100% of Inter. Std.
		Sample: Canadian Standard Digitalis.	
Lethal Frog	Aug. 1928	0.0088 cc. at 0.00000039 Gm.	115% for Ouabain
Lethal Frog	Sept. 1932	0.0075 cc. at 0.0075 cc.	100% of B. P.
Lethal Frog	Jan. 1933	0.0055 cc. at 0.0040 cc.	73% of B. P.
4-Hr. Frog	Nov. 1931	0.0050 cc. at 0.0060 cc.	120% of Inter. Std.
4-Hr. Frog	Feb. 1932	0.0045 cc. at 0.0040 cc.	90% of Inter. Std.
4-Hr. Frog	Apr. 1932	0.0045 cc. at 0.0040 cc.	90% of Inter. Std.
4-Hr. Frog	Dec. 1932	0.0060 cc. at 0.0060 cc.	100% of Inter. Std.
M. S. D. Frog	Apr. 1932	0.0060 cc. at 0.0000006 Gm.	120% of U. S. P. Std.
M. S. D. Frog	Apr. 1932	0.0060 cc. at 0.0000006 Gm.	120% of U. S. P. Std.
M. S. D. Frog	Jan. 1933	0.0055 cc. at 0.0000007 Gm.	152% of U. S. P. Std.
M. S. D. Frog	July 1933	0.0060 cc. at 0.0000006 Gm.	120% of U. S. P. Std.

DISCUSSION.

Assay results by the lethal frog method, which includes also the four-hour method, show that the International Standard digitalis leaves and the Canadian Standard leaves are very nearly equal to each other in activity, as they should be. An average of six tests shows the International Standard to be 107% of the Canadian Standard or that the latter is 93.5% of the former. This is a close enough agreement experimentally to consider them equal.

By the U. S. P. X one-hour method and against the official Ouabain standard the International Standard tincture averages 123% of the U. S. P. in five tests and the Canadian Standard tincture averages 128% of the U. S. P. or nearly the same as the B. P. Since each of these averages contains one or two high results obtained on winter frogs (Jan. 1933) it would seem that the B. P. and Canadian Standard tinctures of digitalis are from 20% to 25% more active than the U. S. P. Standard tincture and that conservatively the difference might be considered as being fully 20%.

By the cat method (two tests) the International Standard seems to be fully 90% of the standard proposed by Hatcher for Tincture of Digitalis but this series of tests is not large enough to prove much except that the B. P. 1932 Standard Tincture of Digitalis is about equal to the Hatcher Standard.

CONCLUSIONS.

1. The standard tincture of digitalis of the British Pharmacopœia, 1932 revision, is fully 20% more active than the U. S. P. X Standard. This difference is significant and is difficult to determine because of the recommended use of different standards and methods of bioassay.

2. The B. P. 1932 Standard tincture and the Canadian Standard, 1928 regulations, Food and Drugs Act are equal, within the limits of experimental error of the methods of assay, as they should be.

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PHYTOCHEMICAL NOTES.*

No. 110. The Sterols from Stramonium Seed.[1]

BY OLE GISVOLD.

The unsaponifiable material obtained by Ralph Clark in his study of the fatty acids of stramonium seed (1) was heated under a vacuum on a water-bath for a half day. It was then allowed to stand for several days in a vacuum desiccator in order to remove any traces of moisture present. Ten grams of this material (2) were dissolved in sufficient alcohol to make 150 cc. of solution. Two and one-half grams of digitonin, Merck, were dissolved in 250 cc. 90 per cent alcohol. Both

* From the laboratory of Edward Kremers.

[1] Scientific Section, A. Ph. A., Toronto meeting, 1932.

solutions were heated to 65° and the digitonin solution was added to the solution of the unsaponifiable material. An immediate separation of the digitonide took place. The mixture was allowed to stand over night and filtered by means of suction. The precipitate was suspended in alcohol, filtered off again and the precipitate washed several times with alcohol and ether.

A test made with the first mother liquor gave a precipitate with digitonin. Therefore, 200 cc. of 1 per cent digitonin solution were added to the mother liquor in the manner previously described. There was no immediate precipitate, but upon cooling the digitonide crystallized out. After standing over night the precipitate was treated as previously described. It is a distinct advantage to thoroughly wash the digitonide as previously described, otherwise oil will be encountered in the crystallization of the sterol. As the solubility of the digitonide is only 0.014 (3) Gm. in 100 cc. alcohol at 18°, the loss of sterol cannot be appreciable. The second mother liquor was concentrated to half its volume, when upon cooling, a third though small quantity of digitonide settled out.

Dried in a desiccator the following weights of the precipitates were determined:

I	2.9809 Gm.
II	1.9030 Gm.
III	0.4014 Gm.
Total	5.2853 Gm. corresponding to 1.321 Gm. of sterol or 13.21 per cent of the unsaponifiable material.

Precipitate No. I, placed in a thimble, was extracted for ten hours with xylene by continuous percolation. The xylene of the resulting solution was evaporated on a water-bath under reduced pressure. The residue left in the flask was then dissolved in ether, alcohol added to the solution and the ether boiled off. A small quantity of charcoal was added to the alcoholic solution and the mixture boiled gently for a few moments with continuous agitation, and then filtered. The alcoholic filtrate of the sterol was reheated and just enough water added until the temporary turbidity thus produced threatened to become permanent. Upon cooling beautiful opaque leaflets were obtained which upon recrystallization, melted at 134° to 135°. The mother liquor yielded crystals m. p. at 127° to 128°. The first crop of crystals was acetylated by boiling gently for one hour with an excess of acetic acid anhydride. Upon recrystallization the acetate melted at 131° to 132°. The acetate was saponified (4) and upon recrystallization the regenerated sterol melted at 137° to 138°.

When treated according to Windaus u. Hauth, the acetate gave no precipitate, indicating the absence of stigmasterol (7).

Burian's sitosterol (5) melts at 137° to 138°, its acetate at 127° to 128°.

Anderson and Shriner (6) have shown that the sterol obtained from corn oil m. p. 137° to 138° can be resolved into γ, β and α sitosterol.

Anderson and Nabenhauer (8), report a highly purified sitosterol m. p. 138° to 139°, the acetate melting at 130° to 131°.

Digitonide precipitates II and III were combined and were subjected to the same treatment as No. I. The recovered sterol crystals were combined with those that had previously been obtained as a second drop of the first batch with a m. p.

127° to 128° because of similarity of m. p. The acetate obtained upon recrystallization melted at 120° to 121°.

The material marked "III A" by Clark was recrystallized. Beautiful almost transparent leaflets were obtained which melted at 135°. Even after drying at 100° over P_2O_5 in a vacuum the melting point was not changed.

The remainder of the unsaponifiable material which amounted to 53 Gm. was treated with digitonin in the manner previously described. The sterol thus obtained exhibited the same physical properties as that obtained before, *i. e.*, the free sterol melted at 138°, and the acetate melted at 131° to 132°.

A mixed melting point was made with the sterol obtained from digitalis seed and no change in the melting point could be noticed. Evidently the two sterols are identical.

The sterol acetate was saponified with alcoholic potassium hydroxide (half normal) by refluxing for one and one-half hours. The excess alkali was back titrated with half normal hydrochloric acid. The values thus obtained indicate that the sterol has the composition $C_{26}H_{43}OH$.

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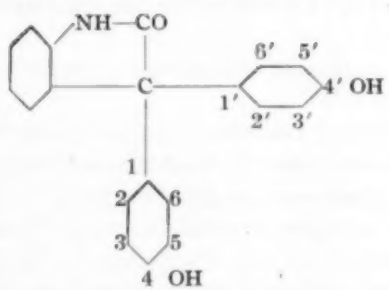
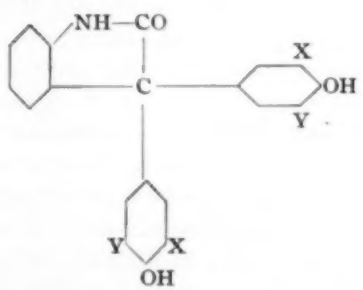
MERCURATED SUBSTITUTION PRODUCTS OF DIPHENOL ISATIN.*

BY S. E. HARRIS AND W. G. CHRISTIANSEN.

The results obtained during our study of mercury derivatives of phthaleins derived from *o*-hydroxy diphenyl (1) suggested that therapeutically valuable mercury compounds should be found among compounds of similar general structure. Diphenol isatin (I) was selected as the parent substance for the investigation and a number of mercury derivatives of the substituted products (II) (Y = NO_2 or Br; X = H, C_6H_5, CH_3, NO_2 or Br) were prepared.



(I)



(II)

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* Scientific Section, A. PH. A., Toronto meeting, 1932.

All of the compounds studied possessed considerable bactericidal properties and the results obtained when they were tested against *B. Typhosus* in aqueous alkaline solution are shown in Table I.

TABLE I.

Diphenol Isatin Derivative.	Highest Dilution Which Kills *B. Typhosus* in 5 Minutes.
Acetoxy mercuri 3,3′, 5,5′ tetrabromo-	1–10,000
Diacetoxy mercuri 3,3′ dibromo-	1–500
Acetoxy mercuri 3,3′ dinitro-	1–30,000
Diacetoxy mercuri 3,3′ dinitro-	1–10,000
Acetoxy mercuri 3,3′ dibromo 5,5′ dimethyl-	1–500
Diacetoxy mercuri 3,3′ dinitro 5,5′ dimethyl-	1–1,000
Acetoxy mercuri 3,3′ dibromo 5,5′ diphenyl-	1–1,500
Diacetoxy mercuri 3,3′ dibromo 5,5′ diphenyl-	1–1,500
Diacetoxy mercuri 3,3′ dinitro 5,5′ diphenyl-	1–1,000
Diacetoxy mercuri 3,3′ dibromo-diresorcin isatin	1–500
Hydroxy mercuri 3,3′ dinitro-diresorcin isatin	1–1,000

The preparation of the intermediates was carried out by introducing the substituent into diphenol isatin prepared by the method of Baeyer and Lazarus (2), in which one molecule of isatin is condensed with two molecules of phenol by adding a small quantity of concentrated H_2SO_4 to a mixture of the two compounds. 5,5′-dimethyl- and 5,5′-diphenyl-diphenol isatin were prepared in the same manner by condensing, respectively, *o*-cresol and 2-hydroxy diphenyl with isatin. It was found that diresorcin isatin could not be prepared in this way, since the high temperature required to melt the resorcin led to an extremely violent reaction with formation of tars. Condensation proceeded smoothly in glacial acetic acid solution, the product being formed without the usual elimination of water between two hydroxyl groups. It was subsequently observed that substitution under mild conditions, *e. g.*, in glacial acetic acid, bromination could be effected without closing the oxonium ring at positions 6 and 2′, whereas nitration in concentrated sulphuric acid led to the elimination of water.

Mercuration was in general effected by the method previously described (1), but in a number of cases this led to the formation of mixtures of mono, di- and trimercury derivatives which we were unable to separate, the compounds being characterized by complete insolubility in organic solvents. Other means of mercuration were adopted in such cases. The compounds obtained were all readily soluble in a slight excess of aqueous alkali. In no case was a melting point observed, the compounds decomposing without melting when heated. The position of the mercury has not been determined. There is ground for belief, however, that in some cases the mercury enters the isatin residue while in others it enters the phenol residue. This, as in the case of the phthalein, is based on the readiness with which disubstitution occurs in certain nitro derivatives, while we have been unable to introduce a second mercury into 3,3′,5,5′-tetrabromo diphenol isatin. This indicates that in acetoxy tetrabromo diphenol isatin a single mercury enters the isatin residue, and that in diacetoxy mercuri 3,3′-dinitro diphenol isatin we have mercury substitution at the 5 and 5′ positions. The high-mercury analyses reported in the experimental part indicates that in the latter compound there is some formation of the triacetoxy mercuri derivative, with the third mercury entering the isatin residue.

Analysis for mercury was carried out by the method of Whitmore (3), but with somewhat unsatisfactory results. As stated elsewhere (1) the method of Tabern and Shelberg (4) is now used in this laboratory.

EXPERIMENTAL.

3,3'-Dibromo Diphenol Isatin.—3.17 Gm. diphenol isatin (2) was suspended in 40 cc. glacial acetic acid and a solution of 3.2 Gm. bromine in 10 cc. glacial acetic acid added dropwise with stirring. The reaction product was isolated by dilution with water, and recrystallized from benzene as a fine white powder.

Melting point—144–145° C.
Yield—88%.
Analysis (Parr bomb) Br—Found 33.92%; 33.24%. Calc. for $C_{20}H_{13}NO_3Br_2$—33.83%.

Diacetoxy Mercuri 3,3'-Dibromo Diphenol Isatin.—General method of mercuration in alcohol solution: 3.5 Gm. of dibromo diphenol isatin was dissolved in 35 cc. alcohol and the boiling solution treated with a solution of 4.7 Gm. of mercuric acetate in 15 cc. water acidified with acetic acid. Stirring and boiling was continued until a side test with NaOH showed absence of ionic mercury. The precipitated mercury derivative was then filtered off and washed with alcohol and ether. It formed a pale yellow sandy powder insoluble in the common organic solvents, readily soluble in dilute alkalies.

Yield—Quantitative.
Hg—Found 41.3%. Calc. for $C_{24}H_{17}NO_7Br_2Hg_2$—42.5%.

3,3',5,5'-Tetrabromo Diphenol Isatin.—48 Gm. diphenol isatin was suspended in 480 cc. glacial acetic acid and 97 Gm. bromine added dropwise with stirring. The mixture was allowed to stand for an hour and then poured into 3 liters of water. A fine greenish precipitate formed which was filtered off, washed with water and recrystallized from alcohol.

Yield—Quantitative. M. p. decomposes above 275° C.
Br (Parr bomb)—Found 50.82%; 50.87%. Calc. for $C_{20}H_{11}NO_3Br_4$—50.56%.

Acetoxy Mercuri 3,3',5,5'-Tetrabromo Diphenol Isatin.—91 Gm. tetrabromo diphenol isatin was dissolved in 144 cc. 2 *N* NaOH and 150 cc. of water. To the boiling solution a hot solution of 46 Gm. mercuric acetate in 20 cc. *N* acetic acid and 150 cc. of water were added, and heating and stirring continued for a few minutes after the addition was complete. The mercury derivative was precipitated as a bluish gelatinous mass, to which 2 liters of water and sufficient NaOH to dissolve the product were added. After filtering off a small insoluble impurity the mercury derivative was regenerated, by the addition of acetic acid, as a thick gelatinous mass, very difficult to filter and wash.

Yield—Quantitative.
Hg—Found 24.3%. Calc. for $C_{22}H_{14}NO_5Br_4Hg$—22.5%.

3,3'-Dinitro Diphenol Isatin.—3.17 Gm. diphenol isatin was suspended in 25 cc. glacial acetic acid and 1.5 cc. HNO_3 (Sp. Gr. 1.4) was added dropwise with stirring. After warming a short time on the water-bath to complete the reaction, the solution was poured into 400 cc. water and the precipitate recrystallized from dilute alcohol.

Yield—3 Gm. M. p. decomposes at 225° C.
N—Found 10.54%; 10.86%. Calc. for $C_{20}H_{12}N_2O_7$—10.37%.

Diacetoxy Mercuri 3,3'-Dinitro Diphenol Isatin.—Mercuration was carried out by the general method. The product was a bright yellow powder.

Yield—Quantitative.
Hg—Found 47.1%; 48.1%. Calc. for $C_{24}H_{17}N_3O_{11}Hg_2$—43.5%.

All methods of preparation gave products with a high and variable mercury content.

Diresorcin Isatin.—5.6 Gm. isatin and 8.2 Gm. resorcin were suspended in 50 cc. glacial acetic acid, and conc. H_2SO_4 added drop by drop with good stirring till the isatin color disappeared and a homogeneous solution resulted. On pouring into 500 cc. water and standing, a fine white powder was precipitated. A suitable solvent for recrystallization was not found.

Yield—6 Gm. M. p. decomposes above 270° C.

Found	C	68.9	H	4.2	N	3.89
		68.8		4.5		4.08.
Calc. for $C_{20}H_{13}NO_5$	C	68.8	H	4.3	N	4.01%.

3,3'-Dibromo Diresorcin Isatin.—7 Gm. diresorcin isatin in 50 cc. glacial acetic acid was treated with 6.3 Gm. bromine dissolved in 10 cc. glacial acetic acid. The product was isolated by dilution with water, and recrystallized from alcohol.

M. p. 250–255° with decomposition.

Diacetoxy Mercuri 3,3'-Dibromo Diresorcin Isatin.—2 Gm. of the dibromo compound was mercurated by the general method with 2.5 Gm. mercuric acetate.

Yield—90%.
Hg—Found 38.4%. Calc. for $C_{24}H_{16}NO_9Br_2Hg_2$—39.2%.

3,3'-Dinitro Diresorcin Isatin.—5 Gm. diresorcin isatin was dissolved in 30 cc. conc. H_2SO_4 and cooled to 0° C. To this solution a mixture of 2.8 cc. HNO_3 and 3 cc. H_2SO_4 was added drop by drop, keeping the temperature at 0° C. After stirring for a further period of 30 minutes the reaction mixture was diluted with 5 volumes of water, the precipitate filtered off and washed. The brown reaction product was very soluble in alcohol and glacial acetic acid but did not separate in a crystalline form on evaporation or dilution. It was insoluble in ether, benzene and chloroform. Decomposed without melting at 220° C.

Yield—Practically quantitative.
N—Found 10.16%; 10.65%. Calc. for $C_{20}H_{12}N_4O_8$ 9.97%.

Hydroxymercuri 3,3'-Dinitro Diresorcin Isatin.—4.2 Gm. 3,3'-dinitro diresorcin isatin was dissolved in 50 cc. *N* NaOH and a hot solution of 6 Gm. mercuric acetate in 25 cc. water acidified with acetic acid added. After standing a short time the mercury derivative was precipitated by adding dilute H_2SO_4, filtered off and washed with water, alcohol and ether.

Hg—Found 32.8%; 32.0%. Calc. for $C_{20}H_{10}N_2O_9Hg$ 31.5%.
Yield—Practically quantitative.

3,3'-Diphenyl-Diphenol Isatin.—20 Gm. 2-hydroxy diphenyl was melted and 5 Gm. isatin suspended in the molten mass, maintaining the temperature at about

60° C. 2 cc. conc. H_2SO_4 was added dropwise and stirring continued until the reaction mixture set to a solid cake. This was then broken up and boiled with water to remove traces of 2-hydroxy diphenyl. The product was purified by recrystallization from alcohol and water or by solution in NaOH and reprecipitation with dilute acid. It forms a white powder, m. p. 183–185° C.

Found	C	82.3	H	4.95	N	2.87; 2.95
Calc. for $C_{22}H_{22}NO_3$	C	81.9	H	4.90	N	3.00%.

3,3'-Diphenyl 5,5'-Dibromo Diphenol Isatin.—31 Gm. 3,3'-diphenyl diphenol isatin, dissolved in 300 cc. alcohol or glacial acetic acid, was treated with 20.5 Gm. bromine dropwise. After standing for a short time the product was isolated by dilution with 1.5 liters water, and recrystallized from dilute acetic acid.

Yield—96%. M. p. 115° C.
Br—Found 27.49%. Calc. for $C_{22}H_{21}NO_3Br_2$ 26.69%.

Acetoxy Mercuri 3,3'-Diphenyl 5,5'-Dibromo Diphenol Isatin.—The dibromo compound on mercuration by the general method gave a brownish sandy powder in quantitative yield.

Hg—Found 22.4%. Calc. for $C_{34}H_{23}NO_5Br_2Hg$ 22.7%.

Diacetoxy Mercuri 3,3'-Dibromo 5,5'-Diphenyl Diphenol Isatin.—The bromo compound was mercurated by the general method using two equivalents of mercuric acetate. The properties resembled those of the mono-mercury derivative.

Hg—Found 36.0%. Calc. for $C_{38}H_{26}NO_7Br_2Hg_2$ 35.1%.

3,3'-Diphenyl 5,5'-Dinitro Diphenol Isatin.—4.7 Gm. 3,3'-diphenyl diphenol isatin was dissolved in glacial acetic acid and treated with 1.5 cc. HNO_3 (Sp. Gr. 1.4). The product was isolated by dilution with water, and recrystallized from alcohol. Yellow needles m. p. 148° C.

Yield—Practically quantitative.
N—Found 7.34%. Calc. for $C_{22}H_{21}N_3O_7$ 7.51%.

Diacetoxy Mercuri 3,3'-Diphenyl 5,5'-Dinitro Diphenol Isatin.—Mercuration by the general method gave a brown sandy powder assaying rather high for mercury.

Hg—Found 44.6%; 44.0%. Calc. for $C_{36}H_{25}N_3O_{11}Hg_2$ 37.3%.

As in the case of dinitro diphenol isatin, all attempts to prepare pure dimercury derivatives gave a partially trimercurated mixture.

3,3'-Dimethyl 5,5'-Dibromo Diphenol Isatin.—13 Gm. di-*o*-cresol isatin (5) prepared in the same manner as diphenol isatin, was dissolved in 125 cc. glacial acetic acid and treated with 13 Gm. bromine. About 30% of the product was precipitated as a micro-crystalline powder while the remainder was obtained on dilution with water. Recrystallized from glacial acetic acid, it formed needles.

Yield—90%. M. p. decomposes 250° C.
N—Found 2.78%. Calc. for $C_{22}H_{17}NO_3Br_2$ 2.79%.

Acetoxy Mercuri 3,3'-Dimethyl 5,5'-Dibromo Diphenol Isatin.—On mercuration in alcohol solution by the general method the reaction appeared to be reversible since long boiling failed to give a negative test for inorganic mercury. The crude

product was freed from the unchanged isatin derivative by repeated extraction with boiling alcohol.

Hg—Found 26.0%. Calc. for $C_{24}H_{19}NO_5Br_2Hg$ 26.4%.

3,3'-Dinitro 5,5'-Dimethyl Diphenol Isatin.—24 Gm. di-*o*-cresol isatin (5) was dissolved in 25 cc. glacial acetic acid and treated with 10 cc. HNO_3 (Sp. Gr. 1.4). After warming on the water-bath for 15 minutes the product was precipitated by adding water and recrystallized from alcohol. Yellow micro-crystalline powder m. p. 238–240° C.

N—Found 9.68%. Calc. for $C_{22}H_{18}N_3O_7$ 9.65%.

Diacetoxy Mercuri 3,3'-Dinitro-5,5'-Dimethyl-Diphenyl Isatin.—The nitro compound when mercurated in alcohol by the general method gave a partially trimercurated product, as in the case of the other nitro derivatives.

Hg—Found 44.7%. Calc. for $C_{24}H_{18}N_3O_9Hg_3$ 43.3%.

SUMMARY.

A number of new derivatives of diphenol isatin have been prepared. The mercury derivatives of these compounds have been prepared and their bactericidal properties investigated.

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RESEARCH DEPT. OF THE CHEMICAL & PHARMACEUTICAL LABORATORIES,
E. R. SQUIBB & SONS, BROOKLYN, N. Y.

THE VALUE OF SENECIO IN MEDICINE.*,[1]

BY EDGAR A. KELLY AND E. V. LYNN.

In a preliminary report two years ago (3) we recorded a partial examination of senecio. Since then we have completed the study and extended it to include the pharmacology.

CHEMICAL.

The material employed was obtained in the open market and was entirely within the official requirements, but we have no knowledge of place or time of gathering.

Proximate analysis of various samples gave results as follows: moisture 6.49 to 10.92 per cent; ash 8.33 to 11.85 per cent; starch, by diastase 7.85, by acid hydrolysis 10.20 per cent; tannin 6.14 per cent.

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* Scientific Section, A. PH. A., Madison meeting, 1933.

[1] Research conducted under the grant of the National Conference on Pharmaceutical Research.

For the purpose of complete examination, 13 Kg. of the ground drug was exhausted with hot alcohol. After removal of the greater part of the solvent, there was obtained 2.67 Kg. of a dark, viscid mass.

Volatile Oil.—By steam distillation of this extract there was produced 13.6 Gm., or 0.1 per cent, of an essential oil which was acid to litmus and possessed the characteristic, aromatic and spicy odor of the drug. It was light amber in color when first obtained but darkened on standing to a reddish brown color, thus exhibiting the presence of unstable compounds. The oil thus changed had the following constants: d_{25} 1.0072; n_D^{20} 1.4942; $[\alpha]_D$ + 27.91°; acid number 52.47; ester value 89.63. It gave no test for nitrogen or sulphur when submitted to the sodium-fusion method; the former report of finding sulphur was probably due to contaminated steam. The previous refraction (1.4511) was obtained with only a few drops of oil.

After rectification by steam, the oil had the following constants: d_{25} 0.9862; n_D^{20} 1.4921; $[\alpha]_D$ + 40.74°; acid number 25.33; ester value 60.47. These indicated unsaturated or aromatic compounds with comparatively large amounts of free acids and some esters.

Aqueous Residue.—The residual, dark brown, aqueous liquid was separated from the resins and evaporated to a convenient volume under reduced pressure. Repeated extraction with ether gave 25 Gm. of semi-solid, from which ammonium carbonate withdrew 16.4 Gm. (0.12 per cent) of oil representing free, non-volatile acids. Sodium carbonate solution extracted 1.15 Gm. (0.01 per cent), more than half of which crystallized in long needles melting at 129–130° C. and which was probably a lactone. It was soluble in benzene, ether, chloroform or hot water, but insoluble in petroleum ether or cold water, and was acid to litmus. From the original ethereal extract sodium hydroxide solution removed 0.41 Gm. (0.003 per cent) of phenols.

From the aqueous concentrate amyl alcohol extracted 32 Gm. (0.25 per cent) of a syrupy material. Most of this remained liquid even after standing for several months, but there separated 0.6 Gm. of a brown, amorphous powder which was apparently an anthraquinone derivative.

In the remaining aqueous product, which represented chiefly sugars, nothing else beside sugars was found. At no time was there any indication of glucosides and no characteristics of a saponin.

The Resins.—The solid portion from distillation amounted to 950 Gm. or about 7 per cent of the original drug. Of this black tarry mass, representing the fixed oil, phytosterol, resin, wax, etc., 18 per cent was removed by petroleum ether and subsequently 15 per cent by ether, both extracts being dark green and unctuous. Chloroform extracted from the residue 14 per cent of a black, brittle solid and alcohol then removed 9 per cent of black semi-solid, these probably being chiefly wax and resin. Nearly half of the original remained as a black mass.

Alkaloid.—In our previous report the presence of alkaloid was indicated. In order to determine this more carefully a large quantity of drug was exhausted with alcohol and the latter was largely removed by distillation. The residue was extracted with 2 per cent hydrochloric acid, producing a brown solution which gave copious precipitates with Wagner's or Mayer's reagents and with phosphotung-

stic acid, phosphomolybdic acid or picric acid, but none with tannic acid, Dragendorff's or Marme's reagents, platinic chloride or gold chloride.

The acid solution was made alkaline and extracted with a mixture of three parts ether and one part chloroform. The dried extracts were combined and evaporated to dryness, leaving a green, mobile oil corresponding to 0.006 per cent of the dried plant. It was acid to litmus and possessed a bitter and burning taste.

Weighed portions of the residue were tested for nitrogen by the sodium-fusion method. Amounts representing as much as 600 Gm. of the crude drug failed to give a positive test. Since, in our hands, as little as 4 mg. of strychnine will give the characteristic blue, and assuming that the proportion of nitrogen is about the same, we conclude that alkaloids are not present in senecio in amounts greater than 1:150,000.

At the time this work was being conducted, Manske (4) was also testing senecio for the presence of alkaloid. His results, which did not include a test for nitrogen, led him to draw doubtful conclusions.

Inulin.—Precipitated calcium carbonate was mixed with 600 Gm. of the crude drug in order to neutralize plant acids and the mixture was introduced into an equal volume of boiling water and heated on the steam-bath. After about four hours it was strained through muslin and expressed. These processes were repeated three times, when the liquid was filtered until clear and the tannins, colors, etc., were precipitated with neutral lead acetate. Basic lead acetate produced no more precipitate. After removing the lead with sodium phosphate the filtrate was reduced to one-third its volume by evaporation under reduced pressure.

Addition of an equal volume of alcohol caused precipitation of a white amorphous substance which was filtered and washed with alcohol and ether. The tasteless substance, resembling starch in appearance, was insoluble in cold water and organic substances but, unlike starch, gave a clear solution in hot water. After purification its solution was neutral to litmus, produced no change with iodine and did not reduce Fehling's solution. After hydrolysis by boiling with dilute hydrochloric acid for one minute, however, it produced an immediate reduction of hot Fehling's solution. A hydrolyzed solution gave a deep red color and a red precipitate when boiled with resorcinol in hydrochloric acid, thus proving the hydrolytic product to be a ketone sugar. The specific rotation was $-38.6°$, of pure inulin $-39.5°$, of soluble starch $+169.1°$. The hydrolytic product had a specific rotation of $-95.7°$, comparable to the $-98.8°$ of levulose. The original substance is thus proved to be inulin, which is present to the extent of about 7.85 per cent.

While inulin is quite prevalent in plants of the composite family, this is the first instance we can find that it has been found in a senecio.

The liquid from which the inulin had been precipitated was evaporated to a small volume under reduced pressure and was then allowed to stand for several weeks, being subject to some evaporation in the meantime. Nothing crystalline was thus obtained and other properties of the residue would seem to indicate that glucosides are either absent or present only in very small quantities.

PHARMACOLOGICAL.

Attempts to isolate and identify compounds to which the reputed value could be attributed having failed, attention was next turned to the pharmacology.

This involved determination of toxicity, action on the excised uterus and on the uterus in a living animal.

Toxicity.—The animals used were two fully grown, healthy, white rats, one male and one female. The fluidextract, administered orally by means of a medicine dropper, was given in increasing doses at intervals of one or two days in order that there would be no accumulation. No effects were noted at any time. Since the largest dose corresponded to 100 times the average for man, the fluidextract can be considered non-toxic to rats.

Weighed quantities of the crude drug were mixed with glucose, rolled into pills and administered to a rabbit weighing 2406 Gm. Three doses were given at intervals of two days. The first, 4 Gm. of senecio, corresponded to 0.17 per cent of the body weight, the second of 12 Gm. to 0.5 per cent and the third of 24 Gm. to 1.0 per cent. In order to get the same amount of drug per Kg., the average adult person would need to ingest 700 Gm. None of these enormous doses produced any outwardly evident effects and it can be concluded that senecio is entirely non-toxic.

Isolated Uterine Strip.—The only previous investigation of this nature on senecio was made by Pilcher in 1916 (2), who finally concluded that the fluidextract gives no constant action on the excised uterus of guinea pigs. In high concentration, however, there was an indication that the drug is depressant.

The animals used were adult, non-pregnant rabbits and cats. The rabbit was killed by a blow on the head, the vessels in the neck were cut and the animal was rapidly bled. The abdomen was opened and the entire uterus, including the ovaries and a part of the vagina, was removed to a beaker containing Ringer-Dale solution. The cats were anesthetized by ether instead of being killed before bleeding.

On a warm, moistened tile, one horn of the uterus was cut longitudinally with sharp scissors and, with the muscle laid flat, a segment was made 1.5 cm. long and 0.5 cm. wide. Holes were pierced in each end to receive pieces of silk thread which were tied securely, one being attached to a muscle lever, the other to a writing lever. The uterine strip, with its attached muscle lever, was then placed in a Harvard warmer containing 50 cc. of Ringer-Dale solution, which was well oxygenated and maintained at about 38° C. by means of an outer water-bath. The jacket of the latter was a galvanized pail in the bottom of which was a hole to receive a rubber stopper. A short glass tube was passed through this stopper and connected by means of a rubber tube to the muscle chamber. The outer end of the glass tube was attached to a T-tube, one arm of which served as a washout for the chamber, the other being connected to a second T-tube. The second arm of the latter led to the oxygen tank and the third to a reservoir of fresh saline kept at 38° C. Thus, by regulating various screw clamps, the solution surrounding the muscle was kept well oxygenated and could be washed out and renewed with fresh, warm saline in a fraction of a minute. The thread from the upper end of the uterine strip was attached to the short arm of a counterbalanced lever which recorded contractions by an upstroke of the writing point on a slowly moving kymograph drum.

After obtaining a satisfactory normal tracing, free from spontaneous and erratic movements, the drug was added at the top of the chamber and away from the

strip by means of a graduated capillary pipette. It was allowed to act for ten minutes or longer. The preparation used was the official fluidextract prepared by Eli Lilly & Co. containing 55 per cent of alcohol, control experiments being run with the evaporated fluidextract, with 55 per cent alcohol and with fluidextract of ergot (Lilly). The results with the evaporated preparation did not differ materially from those of the official one, while the tests with alcohol showed that this ingredient has little effect on the uterine strip. The fluidextract of ergot caused the usual pronounced stimulation in all controls.

The concentrations used were much higher than those which could be produced in the body. If we assume that the average dose, 4 cc., be completely and rapidly absorbed, there would be about 1 : 17000 in the blood of an adult man. In our experiments the concentrations employed were 1 : 1000 and 1 : 500.

Out of a total of ten experiments using a dilution of 1 : 1000, rate and amplitude were increased in one and remained constant in nine. The tonus was raised in two and was unchanged in eight. In the three cases the rises were very small. Out of nineteen experiments using the dilution 1 : 500, the rate was raised in five and lowered in two and the amplitude and tonus were increased in five and decreased in three. Each change, however, was relatively insignificant, being in no case more than a small fraction of the alterations produced by ergot. We may justifiably conclude that even very high concentrations of senecio have no action on the excised uterus.

Intact Uterus.—Since it is impossible to simulate outside the body the conditions which are so rigidly controlled inside the organism, the preceding experiments on excised tissue do not represent the normal effect of the drug. The mode of administration and absorption of the drug, temperature control and oxygen supply and consumption are necessarily greatly changed when the organ is removed. The injury involved in severing the organ from the body and from the nervous mechanism supplying it is a factor not met in studying the activity in the intact animal.

The method of investigation was that of Barbour (1), using fully grown, non-pregnant cats. About one hour was allowed to elapse after the operation had been completed and the apparatus had been adjusted, in order to afford sufficient time for the establishment of regular uterine movements, which were in all cases small. After obtaining a satisfactory record of the normal contractions, the fluidextract was injected in doses of 0.5 cc. through the cannula in the left jugular vein. A control injection of 0.5 cc. of fluidextract of ergot was made at the end of each experiment. In all, five experiments were performed using as many animals. In each fluidextract of senecio failed to change the character of the uterine movements in any respect, while fluidextract of ergot produced the characteristic stimulating action.

CONCLUSIONS.

Although senecio has been used in medicine for many years, chiefly in uterine disorders, we find no published evidence of any value. The drug is official probably because of some considerable usage, but certainly this cannot be because of scientific proof. Since immense doses of the drug give no demonstrable effects on animals, since local application to the uterus gives no action on the rate, amplitude or tone

of the uterine muscle, we are forced to the conclusion that the drug is valueless in the conditions for which it is prescribed. We offer the suggestion that it be eliminated from our materia medica. As long as certain physicians prescribe it, deletion from the formulary may not be deemed advisable, but it would seem logical to urge strongly abandonment of any administration.

SUMMARY.

A proximate analysis of senecio was made, including moisture, ash, tannins, resins, etc. There was found 0.1 per cent of volatile oil whose constants are given, also about 8 per cent of inulin and no starch. No evidence could be found for the presence of alkaloids or glucosides.

Even with enormous doses, senecio caused no untoward effects in rats or rabbits. Numerous experiments on isolated uterine muscle and on normal uterine movements in intact animals clearly demonstrated the absence of any effect on the tone, rate or amplitude of this muscle.

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THE ASSAY OF CAFFEINE SODIO-SALICYLATE AND ELIXIR OF SODIUM SALICYLATE.

BY EDWARD M. HOSHALL, DONALD C. GROVE AND GLENN L. JENKINS.

CAFFEINE SODIO-SALICYLATE.

This preparation has been recommended for admission into the National Formulary VI. A method of assay is proposed.

Assay for Caffeine.—Transfer 2.0 Gm. of caffeine sodio-salicylate, previously dried to constant weight at 80° C., and accurately weighed, to a 100-cc. volumetric flask and make to volume with distilled water. Transfer a 10-cc. aliquot to a separatory funnel, add 5 cc. sodium hydroxide T.S. and extract the caffeine with successive portions of chloroform until the residue gives no test for alkaloids with iodine (T.S.). Pass the chloroform solutions through a filter which has previously been moistened with chloroform and wash the stem of the funnel and filter with a few cc. of the solvent to remove any adhering caffeine. Evaporate the combined chloroform solutions on a water-bath, and dry the residue of anhydrous caffeine to constant weight at 80° C.

Assay for Sodium Salicylate.—Transfer the aqueous liquid from which the caffeine has been removed by the above assay for caffeine to a 500-cc. glass-stoppered Erlenmeyer flask, rinsing the separatory funnel with small portions of distilled water. Also wash the filter and funnel used in the caffeine determination with small portions of water, adding the washings to the 500-cc. flask. Add sufficient distilled water to make the volume in the flask about 100 cc. Add 50 cc. 0.1*N* Bromine solution, 10 cc. of hydrochloric acid, then stopper and shake for one minute, then at intervals for thirty minutes. Add 10 cc. of 15 per cent potassium iodide solution, stopper and shake for five minutes. Titrate the liberated iodine with 0.1*N* sodium thiosulphate solution, using starch T.S. as indicator.

Each cc. of 0.1*N* bromine is equivalent to 0.002668 Gm. $NaC_7H_5O_3$.

Experimental.—According to National Formulary VI *Bulletin*, page 325, the formula and

directions for the preparation of caffeine sodio-salicylate will be the same in the National Formulary VI, as they now are in the National Formulary V. Due to the efflorescent nature of hydrated caffeine, the water content will be extremely variable as shown by W. W. White.[1] Because of this fact it is recommended that the stable anhydrous caffeine (dried at 80° C.) be used for this preparation.

Accordingly the preparation was compounded by following the method as in the National Formulary *Bulletin*, page 525, substituting caffeine dried to constant weight at 80° C., for the hydrated caffeine. The same sodium salicylate as used in the elixir of sodium salicylate was used. The analysis appears in Table II.

The preparation was then assayed by the method given above, with the following results.

TABLE I.

	Analyst.	Amount Present Per Cent.	Amount Found Per Cent.		Error Per Cent.
Sodium Salicylate	A	49.82	49.71	49.74	−0.2
	B	49.82	49.64	49.67	−0.2
Caffeine (dried at 80° C.)	A	50.00	50.01	49.79	−0.2
	B	50.00	49.84	49.77	−0.4

CONCLUSION.

1. Suitable methods of assay for caffeine sodio-salicylate have been developed. It is recommended that the assay be adopted as official in the National Formulary VI.

2. It is recommended that caffeine (dried to constant weight at 80° C.), be substituted for caffeine hydrated, in this preparation.

3. It is recommended that the following tolerances be adopted:

The preparation shall contain not less than 47.5 per cent or more than 52.5 per cent of sodium salicylate.

The preparation shall contain not less than 47.5 per cent or more than 52.5 per cent of caffeine dried to constant weight at 80° C.

ELIXIR SODIUM SALICYLATE.

This preparation has been recommended for admission into the National Formulary VI. A method of assay is proposed.

Assay for Sodium Salicylate.—Transfer 10 cc. of the preparation to a 250-cc. volumetric flask and make to volume with distilled water. Transfer a 10-cc. aliquot to a 500-cc. glass-stoppered Erlenmeyer flask, add 100 cc. of distilled water, 50 cc. of 0.1*N* bromine solution and 10 cc. of hydrochloric acid. Stopper and shake for one minute, then at intervals for thirty minutes. Add 10 cc. of 15 per cent potassium iodide solution, stopper and shake for 5 minutes. Titrate the liberated iodine with 0.1*N* sodium thiosulphate solution, using starch T.S. as indicator.

Each cc. of 0.1*N* bromine = $(0.002668 \times \frac{250}{10} \times 10) = 0.667$ Gm. $NaC_7H_5O_3$ per 100 cc. of solution.

Experimental.—Sodium salicylate (a C.P. quality salt), was assayed by the above method, and also by the extraction and determination of the salicylic acid content. The results are given in the following table.

TABLE II.

	Analyst.	Assay by Proposed Method Per Cent.		Assay by Determination of Salicylic Acid Per Cent.	
Sodium Salicylate	A	99.62	99.62	99.65	99.38
	B	99.76	99.52	99.66	99.57
	Average	99.63%		99.57%	

[1] U. S. P. XI Circulars, General Committee, page 170.

Using the assayed salt and following the method of preparation of Elixir Sodium Salicylate as in the National Formulary VI *Bulletin*, the product was compounded and assayed by the method as presented above. The results appear in Table III.

TABLE III.

	Analyst.	Amount Present Gm./100 cc.	Amount Found Gm./100 cc.	Error Per Cent.
Sodium Salicylate	A		24.77	−0.6
		24.908	24.75	
	B		24.73	−0.6
			24.74	

CONCLUSIONS.

1. A suitable method of assay for Elixir of Sodium Salicylate has been developed. It is recommended that the method of assay herein proposed be adopted as official in the National Formulary VI.

2. It is recommended that the following tolerance be adopted for this preparation: 100 cc. of Elixir of Sodium Salicylate contains not less than 24.5 Gm. or more than 25.5 Gm. of sodium salicylate.

The Pharmacy Exhibit at the Century of Progress will probably be continued this year. Editorial comment is made in this issue of the JOURNAL.

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AROMATIC ELIXIR.*

BY L. D. HAVENHILL AND M. G. SMOLT.

Aromatic Elixir, U. S. P. X is an excellent vehicle and masking agent, one of the best in use to-day. The junior author became interested in the study of this vehicle when large quantities of it were required by the Bell Memorial Hospital in Kansas City, Kansas, and the Watkins Memorial Hospital in Lawrence, Kansas.

The difficulty in preparing this elixir is to secure a clear product. The official process is long and tedious and often disappointing to the busy hospital pharmacist. Several writers, Shiflett (1), Silver (2) and Burlage (3) and others have given the matter of a rapid method of preparing this elixir considerable attention, but their methods in our hands have not been entirely satisfactory.

The volatile oils used in the preparation of the Compound Spirit of Orange from which the Elixir is prepared are shown in Gildemeister and Hoffman (5) to consist, with the exception of Oil of Anise, largely of terpenes which are not readily soluble in a dilute alcohol. These are almost completely precipitated in the preparation of the elixir and are the chief cause of the difficulties encountered.

The oxygenated principles of these oils are the desirable ones. They are also not the ones which cause the cloudiness. The problem resolves itself into the following:

First, to determine a strength of alcohol that can be used in preparing Compound Spirit of Orange that will extract sufficient oxygenated principles from the volatile oils used, but not enough of the terpenes to precipitate on dilution when preparing the aromatic elixir.

Second, to establish the strength of this new spirit as compared with the one now official regarding oxygenated principles.

Third, to ascertain the relative amounts of oxygenated principles present in Aromatic Elixir.

Fourth, to calculate the amount of this "soluble" Spirit necessary to make an Elixir similar in flavoring strength to the one at present official.

A search through the literature yielded very little of value. The articles for the most part were concerned with improving the methods of filtering or with changing the proportions of ingredients used. Krantz and Carr (6) (7), in two articles recorded results using filtering agents other than talc. In actual experience talc has been found to be the most satisfactory filtering medium.

It is reasonable to expect that if a mixture of volatile oils is added to a diluted alcohol, two phases will result. Since the mixture of oils contains oxygenated principles which are also soluble in the diluted alcohol used, an equilibrium will be established in the aldehyde strength of the two immiscible liquids. The amount of oxygenated principles present in the alcoholic phase will depend on both the volume of the solution and the strength of alcohol used. The amount of oxygenated principles remaining in the oil phase is lost in all methods of preparation because this phase is removed through filtration.

Shiflett (1) and Silver (2) claim the products obtained by their methods are identical in strength with Aromatic Elixir, U. S. P. because the same amounts of ingredients have been used, although both processes involve a preliminary pre-

* Section on Practical Pharmacy and Dispensing, Madison meeting, 1933.

cipitation of the hydrocarbon principles of the volatile oils, which are filtered out before adding the remainder of the ingredients. This would lead one to think that the "order of mixing" made no difference in the strength of the finished product.

Experiments were carried out which showed that the amount of oxygenated principles removed by the alcoholic liquid varies considerably with the procedure used. It would seem essential, therefore, when suggesting modifications of the official process, that the quantity of oxygenated principles in the finished elixir be comparable to that in the official elixir. This can only be done by assay. Extensive experiments were made in an effort to get a "soluble" Compound Spirit of Orange.

The method used follows:

Varying amounts of Compound Spirit of Orange were introduced into a 50-cc. volumetric flask and diluted to the mark with distilled water. Each portion was then filtered, using talc, and portions of the filtrate used in compounding small amounts of aromatic elixir. It was found that if 32 cc. of Compound Spirit of Orange, U. S. P. be diluted with distilled water to 50 cc., the resulting mixture thoroughly shaken and filtered, using 10 Gm. of talc, portions of the filtrate, could be compounded into Aromatic Elixir giving a clear product of superior fragrance and taste, which does not require a final filtration. The entire operation of compounding, using the "soluble" Compound Spirit of Orange, takes less than 5 minutes.

The next step was to ascertain the strength of the oxygenated principles of the filtrate as compared with the original spirit.

The method of aldehyde assay proposed by Gfeller (4) was rejected because the terpene constituents are determined as well as the oxygenated principles. The method of Klebler (5) with several variations was tried and rejected because of the difficulty in securing a definite end-point in the residual titration. The colorimetric methods of the A. O. A. C. (8) were also tried. The sulphite-fuchsin method was rejected because the alcohol used gave a color varying with the strength of the alcohol. The method using *M*-phenylene-diamine proved to be suitable and the following modification was used throughout in the subsequent determinations.

Freshly prepared alcoholic solutions of *M*-phenylene-diamine hydrochloride produce no color with the minute amount of aldehydes present in ethyl alcohol. (This reagent must be freshly prepared, for in a few hours it becomes badly discolored and is unfit for use.) The method of comparison used was to pipette 10 cc. of the alcoholic solution to be tested into a 25-cc. volumetric flask and dilute to the mark with a one per cent alcoholic solution of *M*-phenylene-diamine hydrochloride. The color developed was compared, using a colorimeter, with a standard solution similarly prepared. To compare the amount of oxygenated principles in the Compound Spirit of Orange used, with that present in the aromatic elixir made from it, the following method was used.

One and two-tenths cc. of Compound Spirit of Orange were diluted to 100 cc. with 95% alcohol. Another portion of 1.2 cc. of Compound Spirit of Orange with enough alcohol added to make 25 cc., was diluted to 100 cc. with water. (Procedure of the U. S. P. X for Aromatic Elixir, minus the syrup which would cause complications with the aldehyde reagent. It is believed that the presence of sugar does not materially affect the solubility of the oxygenated principles of the volatile oils.) Talc was then added and the product filtered. The aldehyde strengths of the two solutions were then compared by the method given. Comparison was also made of the aldehyde strength of the Compound Spirit of Orange of the U. S. P. X and the

Soluble Compound Spirit of Orange. Since the amount of the Soluble Compound Spirit of Orange used in making the elixir is the amount present in the finished product, as none is lost by filtration, the volume of the "soluble" Compound Spirit of Orange required will be that which contains the same amount of oxygenated principles as is found in 1 liter of Aromatic Elixir, U. S. P. X. Careful comparisons showed that the approximately 25% alcohol dilution of the Compound Spirit of Orange, representing Aromatic Elixir, retained but 44% of the aldehyde strength of the Compound Spirit of Orange used, and that the "soluble" Compound Spirit of Orange had an aldehyde content of but 33% of that of the Compound Spirit of Orange. By simple calculation it is evident that approximately 16 cc. per liter of the soluble Compound Spirit of Orange must be used to duplicate the aldehyde strength of the present official aromatic elixir.

The following formulas are offered for preparing a "soluble" Compound Spirit of Orange from the official spirit, for use in making aromatic elixir.

SOLUBLE COMPOUND SPIRIT OF ORANGE.

Compound Spirit of Orange, U. S. P. X	640 cc.
Talc	30 Gm.
Distilled water	365 cc.

Mix the liquids in a large separatory funnel. Shake thoroughly and allow to stand one-half hour. Draw off the cloudy lower liquid, thoroughly mix it with the talc and filter in the approved manner to secure a clear filtrate and to restrict evaporation.

If the use of the oils is preferred to the Compound Spirit of Orange, the following formula is suggested for making the "soluble" Compound Spirit of Orange.

SOLUBLE COMPOUND SPIRIT OF ORANGE.

Oil of Orange	128 cc.
Oil of Lemon	32 cc.
Oil of Coriander	12.8 cc.
Oil of Anise	3.2 cc.
Alcohol	465 cc.
Water	370 cc.
Talc	30 Gm.
To make about	750 cc. of "soluble" Compound Spirit of Orange.

Mix the liquids thoroughly in a separatory funnel of suitable size. Allow to stand for one-half hour. Draw off the cloudy lower liquid, mix it with the talc and filter in the approved manner to secure a clear filtrate and to restrict evaporation.

The chief use of Compound Spirit of Orange is for preparing Aromatic Elixir. In a few instances it is used in prescription compounding for flavoring. It is believed that this "soluble" compound spirit of orange will prove to be an unobjectionable substitute and much more suitable for use in flavoring medicinals which are low in alcoholic strength.

The following formula is offered for an aromatic elixir which meets the U. S. P. X requirements, using the "soluble" Compound Spirit of Orange.

AROMATIC ELIXIR.

Compound Spirit of Orange, soluble	16 cc.
Syrup	375 cc.
Alcohol	250 cc.
Distilled water	380 cc.
To make about	1000 cc.

Mix the soluble compound spirit of orange with the alcohol. Add the syrup in small portions, mixing well after each addition; then in like manner add the distilled water. (The product at this stage is full of minute bubbles, but clears in a few minutes.)

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A STUDY OF VEHICLES FOR MEDICINES.*

BY BERNARD FANTUS, H. A. DYNIEWICZ AND J. M. DYNIEWICZ.

III. ELIXIR OF PHENOBARBITAL.

If the slogan "Every N. F. preparation a pharmaceutic masterpiece" be adopted, it ought to add immeasurably to the prestige and popularity of its formulas with the medical profession. It may take quite some time to rectify the errors of omission in this respect in the old formulas of this Book, many of which, all will agree, could be improved. We should, however, scrutinize all new formulas that seek admission to this publication from that standpoint. Without pretending to crown the formula we are about to propose as "a masterpiece;"—it is not for us to pronounce it as such—we would like to submit it in competition with other formulas for consideration, most especially, from the standpoint of palatability.

The principle underlying the elaboration of this formula is best illustrated by the following experiment:

1. 0.030 Gm. of Phenobarbital dissolved in 15 cc. of alcohol (95%).
2. 0.030 Gm. of Phenobarbital dissolved in 15 cc. of dilute alcohol (50%).
3. 0.030 Gm. of Phenobarbital dissolved in 15 cc. of 25% alcohol.

It will be found that the taste of Solution 3 is much more bitter than that of Solutions 2 and 1. Of course, Solution 1 is unpleasantly strong in alcohol; and, therefore, one does not hesitate in deciding that Solution 2 gives the best result. The reason for the lower degree of bitterness of the stronger alcoholic solution over the weaker, evidently lies in the physical fact that *a substance will not exchange a good solvent for a poor solvent.* Inasmuch as phenobarbital is so much more soluble

* From the Laboratory of Pharmacology of the University of Illinois.

alcohol than in water, the 50% alcohol is a much better solvent than is the 25% alcohol: and the saliva-saturated mucosa of the tongue and palate is a still poorer solvent. If one desires to test in this case, the validity of the proposition that "*the best solvent is the best vehicle*" all one needs to do is to dilute the solution resulting from Experiment 2 with water, which immediately brings out a great bitterness. Therefore, when the dose is given in this way, it should not be diluted with water.

We secured a rather "delicious" preparation, tasting more like a "liqueur" than medicine, by dissolving a 0.015 Gm. dose of phenobarbital per teaspoonful of 2 parts of "aqueous elixir" to 1 part of "alcoholic elixir." This mixture of solvent would carry even 0.03 Gm. per teaspoonful; but the resulting solution becomes quite bitter. It might be prepared extemporaneously by dissolving the active agent in a mixture of aqueous and alcoholic elixirs, the formulas for which have been previously submitted (article II of this series). It might seem best, however, to present the following formula for its direct preparation:

ELIXIR PHENOBARBITAL.

Elixir of Phenobarbital.

Elix. Phenobarb.

Phenobarbital	**3.75 Gm.**
Gluside	**1.5 Gm.**
Compound Spirit of Orange	**7.0 cc.**
Alcohol	**300 0 cc.**
Glycerin	**200.0 cc.**
Water	**410.0 cc.**
Sucrose	**170.0 Gm.**
Tincture of Cudbear	**6.0 cc.**

Add the compound spirit of orange to the previously mixed solvents. Agitate and permit to stand for 24 hours, with occasional agitation. Filter through a hard filter and dissolve the phenobarbital, gluside and tincture of cudbear in the filtrate: and finally the sucrose, either by solution or percolation and add enough of the mixed solvents to make the product measure 1000 cc.

CONCLUSIONS.

1. An elixir of phenobarbital should be of rather high alcoholic strength, approximately 30%.

2. The dose should not be diluted before taking, as dilution brings out the bitterness.

3. A formula is offered for comparison with others submitted.

4. If the formula be adopted, it might be prepared either directly as stated, or else indirectly by dissolving the required dose in a mixture of 2 parts of the "aqueous" to 1 part of the "alcoholic elixir," the formulas for which have been previously submitted.

IV. ELIXIR OF AMIDOPYRINE.

In constructing a formula for an Elixir of Amidopyrine that might be as palatable as possible, we have tried the following vehicles, dissolving 0.150 Gm. ($2^1/_2$ gr.) of amidopyrine per teaspoonful, which is one-half of the official average dose:

Aromatic Elixir
Iso-alcoholic Elixir, 50%
Compound Elixir of Taraxacum
Elixir of Glycyrrhiza
Elixir Bitter Almond Comp.—made with 50% alcohol
An Alkaline Elixir of Eriodictyon—made with 50% alcohol
Syrup of Glycyrrhiza
Aromatic Syrup of Eriodictyon

In comparing the tastes of these preparations it seems evident to us that the alcoholic vehicles are better than the aqueous vehicles, and that the stronger alcoholic vehicles are superior to those weaker in alcohol. This is as might be expected from the fact that the amidopyrine is much more soluble in alcohol than in water; and it might serve as another illustration of the proposition that "the best solvent is the best vehicle."

In comparing elixirs of analogous alcohol concentration, we find that an alkaline elixir of eriodictyon made with 50% alcohol provides by far the best disguise, subduing the bitterness to a greater extent than any of the others. That this is not merely due to solvent power is evidenced from the fact that the bitterness is not brought out by dilution, as does occur when the previously proposed Elixir of Phenobarbital (4th Communication) is diluted with water. It must, therefore, be due to specific adsorption of the amidopyrine by the eriodictyon resin.

We have proof, by test-tube experiments, that such adsorption actually occurs. When we add 1 cc. of fluidextract of eriodictyon to portions of 5 cc. and 10 cc. of a solution of 1:1000 of amidopyrine, we obtain a colloidal precipitate which is very difficult to remove from the liquid. After clarification with dilute sulphuric acid, it is readily demonstrated by means of Mayer's Reagent that about nine-tenths of the amidopyrine has been taken out of solution. We therefore know that eriodictyon resin combines with amidopyrine. That this combination will be active in the system is made evident by the fact that the precipitate dissolves in $N/100$ HCl, which is about one-fifth the hydrochloric acid strength of the average gastric juice.

We, therefore, respectfully submit the following formula for consideration for possible admission to the National Formulary:

ELIXIR AMIDOPYRINÆ.

Elixir of Amidopyrine.

Elix. Amidopyrin.

Oil of Bitter Almond	**0.5 cc.**
Vanillin	**1.0 Gm.**
Gluside	**1.5 Gm.**
Amidopyrine	**37.5 Gm.**
Fluidextract of Eriodictyon	**30.0 cc.**
Solution of Potassium Hydroxide	**27.5 cc.**
Alcohol	**500.0 cc.**
Syrup	**350.0 cc.**
Orange Flower Water, a sufficient quantity,	
To make	**1000.0 cc.**

Dissolve the oil of bitter almond, the vanillin and the gluside in the alcohol, then add the syrup. Mix. Dissolve the amidopyrine in the above solution.

Mix the fluidextract of eriodictyon and the potassium hydroxide solution; add it to the amidopyrine solution and mix. Finally add enough orange flower water to make 1000 cc.

The above given formula has been constructed with the N. F. Elixir of Bitter Almond as a basis, this having been selected because bitter almond is in itself a good disguise for the bitter taste. We have fortified the elixir by the addition of fluidextract of eriodictyon because of its power of disguising alkaloids and similar bodies, such as amidopyrine. The quantity of fluidextract of eriodictyon has been chosen at the maximum that will still be pleasant. A greater proportion would develop the inherently unpleasant taste of the yerba santa to an offensive degree. The addition of the potassium hydroxide is necessary to secure a clear solution.

We believe that an elixir of the composition elaborated for the disguise of the amidopyrine might also be useful for other similar medicines. We, therefore, would like to submit the following formula for consideration as a possibly useful strongly alcoholic vehicle for alkaloids:

ELIXIR ERIODICTYI ALKALINUM.

Alkaline Elixir of Eriodictyon.

Elix. Eriodict. Alkal.

Oil of Bitter Almond	**0.5 cc.**
Vanillin	**1.0 Gm.**
Gluside	**1.5 Gm.**
Fluidextract of Eriodictyon	**30.0 cc.**
Solution of Potassium Hydroxide	**27.5 cc.**
Alcohol	**500.0 cc.**
Syrup	**350.0 cc.**
Orange Flower Water, a sufficient quantity,	
To make	**1000.0 cc.**

Dissolve the oil of bitter almond, the vanillin and the gluside in the alcohol, then add the syrup. Mix.

Mix the fluidextract of eriodictyon and the potassium hydroxide solution and add to the above solution. Finally, add enough orange flower water to make 1000 cc.

In suggesting the desirability of introducing this elixir of eriodictyon, we would like to point out that we have not reversed our opinion regarding the desirability of deleting the now official elixir. We recommend this deletion because the "Aromatic Elixir of Eriodictyon" is practically not prescribed at all. It is a most unstable preparation in that it precipitates continually. It is an irrational preparation in that a considerable and undeterminable proportion of the active disguising principle of eriodictyon, the resin, is unceremoniously filtered ou... It also suffers from a redundancy of ingredients, containing as many as th..teen, several of them without any good and sufficient reason or advantage. We found that the official elixir contains neither enough alcohol nor of the resin of eriodictyon to give nearly as satisfactory a result in disguising of amidopyrine as the above

proposed elixir, for which the name "Alkaline Elixir of Eriodictyon" might be suggested in order to distinguish it from the elixir at present official.

CONCLUSIONS.

1. An elixir of amidopyrine should be a strongly alcoholic elixir, about 50%, because amidopyrine is more soluble in alcohol than in water.

2. The presence of eriodictyon resin in alkaline solution greatly increases, by adsorption of the amidopyrine, the disguising power of an elixir intended to carry it.

3. An elixir of eriodictyon which serves so admirably as a vehicle for this alkaloid-like body, might also be useful as a vehicle for other similar agents; and its consideration for possible inclusion in the National Formulary, under the title "Alkaline Elixir of Eriodictyon," is suggested.

THE NEW YORK STATE PHARMACY SYLLABUS.*

BY C. W. BALLARD, PHAR.D., PH.D.

The Pharmacy Law of New York State provides for the granting of four degrees in pharmacy. The graduate in pharmacy, Ph.G., is conferred upon the completion of a three-year course with a minimum of 750 hours yearly; the pharmaceutical chemist, Ph.Ch., a three-year course of 1000 hours yearly; the bachelor of science in pharmacy, B.S.Phar., was originally a four-year course of 1000 hours yearly but is now on a semester-hour basis with a minimum of 3600 clock hours; the doctor of pharmacy, Phar.D., representing two years of graduate study subsequent to the attainment of the bachelor's degree. Graduates of both three-year courses are eligible for licensing before the Board of Pharmacy.

The recently issued Pharmaceutical Syllabus IV contemplates a four-year course and is manifestly not applicable to a course of three years' duration. In view of this situation the New York State Education Department has prepared a three-year schedule and syllabus which represents a modification of the Pharmaceutical Syllabus IV. The four-year course, in operation for several years in New York State, is retained and the National Syllabus might have been adopted for this course if it had fulfilled the requirements of the Education Department for the bachelor's degree. The specifications adopted for this four-year course may be briefly stated as follows: 1. It must include all the subjects and hour allotments of the three-year course; 2. It must include a minimum of 3600 clock hours instruction over four calendar years; 3. The division of subjects shall approximately represent fifty per cent each of professional and nonprofessional work; 4. The course shall extend over five days weekly in each calendar year. These requirements, especially the second, necessitated the preparation of a statement of the hours and subjects to be required in both the three- and four-year courses. This syllabus

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has now been published and will presumably be in effect with classes entering in September 1933.

There are naturally many points of similarity in the two syllabi and the major points of difference are due to the specifications previously mentioned. The New York Syllabus adopts three primary divisions of subjects—professional, required academic and required electives as contrasted with the professional or applied and basic groups of the National Syllabus. Certain subjects included in the basic group of the National Syllabus and therefore without detailed statements of the content of the course, are considered as professional subjects in the New York Syllabus and teaching outlines are provided. The subjects are botany, physiology and first aid and elementary physics together with general, inorganic, qualitative, quantitative and organic chemistry. In the New York Syllabus there is a frequent grouping or bulking of time for several related subjects thereby permitting the instructor to apportion the time for each as he sees fit. Every subject listed in the New York Syllabus is required but in the history and elective science groups maximum and minimum limits are stated. In the New York Syllabus the requirements are stated in terms of didactic, laboratory and semester hours excepting in zoölogy, college physics, bacteriology and elective science which are stated in terms of semester hours or points. As regards total time for the courses, the National Syllabus provides for a four-year course with a minimum of 3000 hours, 2336 of required subjects and 664 of optional subjects while the New York Syllabus for the corresponding course requires a minimum of 168.5 semester hours and states a maximum of 183.5 semester hours. Obviously the conversion of semester hours to clock hours depends upon the amounts of didactic and laboratory instruction, but the minimum of 168.5 semester hours is to be equivalent to 3600 clock hours.

The requirements of these two Syllabi, as regards subjects and time allotments, are presented in the following tabulation. It has not been possible to follow the arrangement of either syllabus in compiling this data but it will serve for general purposes of comparison.

	National Syllabus.				New York Syllabus.			
Subjects.	Didactic.	Laboratory.	Sem. Hours.		Didactic.	Laboratory.		Sem. Hours.
Commercial Group.								
Accounting	32	64	O	4	80	64	*R	7
Economics	96	...	R	6				
Jurisprudence	32	...	R	2				
Medical Appliances	...	...	..	..				
Merchandising	64	64	O	6				
Pharmacy Group.								
Arithmetic	32	...	R	2	64	...	*R	4
Dispensing	64	128	R	8	...	352	*R	11
Manufacturing	...	96	O	3	...			
Operative	64	128	R	8	...			
History	32	...	R	2	...	...	..	...
Technic	...	64	R	2	...	...	..	...
Theory	192	...	R	12	320	...	*R	20
Latin	32	...	R	2	32	...	*R	2

Chemistry Group.								
General	48	64	R	5	192	336	*R	32.5
Inorganic	32	64	O	4				
Qualitative	48	64	R	5				
Quantitative	32–48	64	R	4–5	64			
Organic	96	128	R	10	96			
Pharm. Organic	48	64	O	5	...	...	..	...
Biochemistry	48	64	O	5	...	...	..	...
Pharmacology Group.								
Pharmacology or Materia Medica including Toxicology, Posology	96	32	R	7	272	96	*R	20
Microbiology	...	...	..	..				
Pharmacognosy Macro.	64	64	R	6				
Pharmacognosy Micro.	16	64	O	3				
Bioassaying	16	48	O	2.5	...	...	..	...
Insecticides	32	...	O	2	...	...	..	...
Public Health	48	...	R	3	...	...	..	...
Allied Science Group.								
Bacteriology	32	64	R	4			R	3
Botany	64	64	R	6	64	96	*R	7
Physiology	48	48	R	4.5	80	...	*R	5
Physics	64	128	O	8	*64	128	R	8
Zoölogy	32	64	O	4			R	4
Elective courses in science	...	...	..	..			R	9–18
Academic Group.								
English	96	...	R	6		...	R	12
Modern Language	96	...	O	6		...	R	12
History and Social Science	...	...	..	..			R	6–12
Mathematics	96	...	R	6			R	6
Total Required				111.5				168.5
Total Optional				52.5				15.0

R = required; O = optional; * = required in three-year course (110.5 hrs.).

COLUMBIA UNIVERSITY,
COLLEGE OF PHARMACY.

JOHN TENNENT AND SENECA RATTLESNAKE ROOT.*

BY RALPH BIENFANG.[1]

"Traduced, circumvented and at last betrayed: bereft of every consolation, save that of conscious integrity, and a distant hope derived therefrom: I take this method of submitting myself to the determination of the public, in confidence of

* Section on Historical Pharmacy, A. PH. A., Madison meeting, 1933.

[1] From a thesis submitted in partial fulfilment of the requirements for the Ph.D. degree, Univ. of Wisconsin, 1929.

obtaining a sentence agreeable to its usual candour, and suitable to my own deservings, as they shall occur in the subsequent narrative."

Truly a sad statement, but one to be expected since the author was in jail, awaiting trial for bigamy. It was written by John Tennent, discoverer of the use of Seneca rattlesnake root in the cure of pleurisy, as he sat behind bars in the Old Bailey in London in 1742. Jail was not new to Tennent at this time, but let us take up his life where we have the first notice of him.

He bobbed up in Virginia about the year 1728, purporting to have come from Scotland. In the colony, he engaged in the practice of medicine without, however, being in possession of a medical degree. Apparently, he lived a rather unobtrusive life there until 1736. In that year he published in Williamsburg an "Essay on the Pleurisy," announcing his discovery of the use of Seneca rattlesnake root in the cure of pleurisy, and giving at great length the reasons for his coming to the conclusion of its value in that disease. Up to this time, Seneca rattlesnake root had been known only as an Indian remedy for snake bite, it being a very common practice for Braves to carry some of the powdered root in a pouch at the waist for emergency use. Tennent noticed, as he says, a similarity in the symptoms caused by snake bite and by pleurisy, and was actuated by these observations to make use of the root in his pleuritic cases.

His own words were:

"Again as I have observed before, since we are to infer the sameness of causes from the likeness of effects, there is another reason why it should be done in this case, and that is, that those who have the misfortune to be bit by a rattlesnake, do spit up blood, and cough like pleuritic patients: therefore it is beyond all controversy, that the blood of a pleuritic patient, and that of one bit by a rattlesnake is in the same state or very near it. Upon this certainty of reasoning, I gave the rattlesnake root to several patients in a pleurisy or peripneumony, and its effects were extraordinary: I found it to exceed the volatile salt of vipers, or anything that I ever knew given in that disease: In short it may justly be deemed a *Certain Remedy*."

Tennent also made use of the columns of the *Virginia Gazette*, a weekly of that time, in the furthering of his discovery. This, however, seemed to be too great an affront to the regular physicians of the colony, who proceeded to ridicule his reasoning under a pseudonym in the same paper. This went on for about two years, during which time, Tennent made several trips to London.

On his first, he took the "Dorsetshire," leaving June 26, 1737. Through recommendations from friends in Virginia, he was able to get an interview with Doctors Tho. Pellet, R. Mead and Jo. Monro. These men after hearing his story, recommended him for the degree of Doctor in Physic at the University of Edinburgh. This degree he never received, but we have it in his own words that the worth of the practitioner is of the greater importance.

Tennent seems to have been a little overzealous in putting up a front in London for soon he was involved in debt. He returned to Virginia and petitioned the House of Burgesses for a reward for having made public his discovery. This body's first action was refusal, but later it reconsidered, and Tennent was voted the sum of £100. He had expected at least £1000 and was quite disappointed. Real disappointment came when two of his American creditors, Charles Carter and Messrs. Hanner & King, appealed to the House for the reward and got it.

Tennent then managed to return to London. There he proceeded to become

more deeply involved in debt, and during this time had as his common law wife, Elizabeth Cary. Seeking a way out of his financial difficulties, he appealed to Lord Cathcart for the appointment as Physician General to His Majesties Forces in the West Indies. He recommended himself on the strength of his knowledge of the diseases of the country. He failed in this, and his offer to go as assistant to the Physician General was likewise refused.

Now, Tennent had arrived at a position where he would either have to go to jail or leave England, and it was at this crucial time that a friend, Mr. Christian, suggested to him that he marry a lady of fortune, and thus recover his position. Tennent took to this suggestion gladly. The desired woman was found in Mrs. Hanger, a widow of some circumstance, who possessed among other things, an annuity of £50. The marriage was arranged for and took place at St. James Church on Sunday, November 8, 1741, the service being read by Reverend Mr. Fisher.

Three weeks after the marriage, Tennent was lodged in jail for non-payment of debts. He managed to borrow enough to satisfy his creditors, and so was released. Soon after, he was incarcerated again, and this time after getting out, he made an unsuccessful attempt to sell Mrs. Tennent's annuity. Again arrested, for not paying a debt of £12, and again released, he found upon returning home that his wife had left him, quite probably on the advice of one of her brothers, Mr. Parrat, an attorney-at-law, who couldn't stomach among other things, the attempted sale of his sister's annuity.

Distracted, Tennent fled to Scotland, but Mr. Parrat apparently had not finished with him. The facts of his common law marriage were uncovered, and on June 8, 1742, a warrant was granted for the seizure of Tennent wherever he resided. Consequently, he was brought back, and it was after he had been indicted, and was awaiting trial in his cell in the Old Bailey, that he aired his case in a printed pamphlet.

Here the picture dims, and then it ends, with a simple notice in the *Gentleman's Magazine* of Tennent's death in London, on October 27, 1748.

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HISTORICAL PHARMACY IN MINNESOTA.*

BY FREDERICK J. WULLING.

In its seventy-five years of statehood Minnesota has done very well in the recording of historic matters. The Territorial Pioneers organized themselves long ago and the Minnesota Historical Society came into being in territorial days way back in 1849. Later with state aid a half million dollar building for collecting and preserving authentic records of historic interest and value was erected for the

* Section on Historical Pharmacy, A. Ph. A., Madison meeting, 1933.

Society. Histories of many of the cities and counties of the state have been written and some published; not a few in book form, and recently Dr. William Watts Folwell, the first president of the University of Minnesota, in the period during which he enjoyed the honor of the *Emeritus* presidency wrote an exhaustive four-volume history of the state, which no doubt will always remain an authoritative historical reference for the period it covers. Much could be said of the work and accomplishments of the State Historical Society, but it is my purpose only to convey the fact that Minnesota is fairly well off in recorded historical material.

For many years now I have made periodical researches into this material and although I often searched especially for facts of pharmaceutical interest, the field was found almost barren. Here and there a local historian mentions a drug store. Until very recently I have not found a pharmacist among those who have written historical articles or records relating to Minnesota.

This fact and my long association with pharmacists, physicians, dentists and scientists in other fields, led me to the conclusion that the type of mind represented by scientists is not greatly interested in history and that as far as pharmacy is concerned a wider interest in history, at least in its pharmaceutical aspect, should be aroused.

As a result of this conviction the Historical Committee of the Minnesota State Pharmaceutical Association was created a few years ago; that is, the members did not object to the addition of another committee to the list of other practically inactive committees. The next endeavor was to make the committee effective. Charles T. Heller, well-known pharmacist of St. Paul, who was the committee chairman, was the only productive member. However, the seed was sown to arouse a history consciousness among pharmacists. Now after several years of preliminary and preparatory work this committee has been enlarged to represent the various divisions of the state. Possibly to reward or punish me, neither of which I deserve for my persistency in the matter, I have been made chairman of the committee.

It is now certain the committee will do some worth-while work. It will be organized toward that end. While I have some definite plans to produce effective results, suggestions likely to increase the efficiency of such a committee are invited from my hearers or readers.

It would take too much space to repeat all of the instruction and advice given to committee members, but the essential things every member is especially asked to do are to connect events with exact dates, names and localities, get corroborative evidence wherever possible and write down every detail available concerning any event, item or thing of pharmaceutic interest, leaving it to the skilled historian to decide what is essential to select for a representative record.

The committee already has the promise of coöperation of the Minnesota Historical Society and one of the joint objectives is the reproduction of a pioneer drug store in the Historical Building.

The College of Pharmacy already possesses the nucleus of a pharmaceutical museum, which is slowly developing through acquisition of items purchased out of the proceeds of the Wulling Fund established for that purpose. The College, too, will coöperate with the Historical Society and with the Association committee. The museum recently acquired what was represented as the counter scale used in

the first or in one of the first pioneer drug stores in Minnesota. The scale is still in fairly good condition and may be placed in the proposed pioneer drug store reproduction. There are also available in the museum old medicine saddle bags used over a hundred years ago, a blood letting instrument, old wooden iron and brass mortars, plaster irons, four very old show globes, drug and spice grinders, infusion pots, drug jars, old engravings, etc. The museum has just acquired a Chinese medicine cooker over three hundred years old and now very rare. Negotiations are under way for the acquisition of an old sailing vessel's medicine chest.

Work of this sort is no doubt being done in other states or sections of the country. If similar agencies could be organized and be made to work in every state, coming historians would feel grateful, not to speak of the real service that would thus be assured pharmacy in general. It could well come within the province of this Historical Section of the A. PH. A. to advocate and stimulate such activities in every state.

Lithuania.—In towns pharmacies must be kept open until 9:00 P.M., and if there are several pharmacies in a locality the night service is fixed by rota from 9:00 P.M. to 9:00 A.M. Country pharmacies must be open from 9:00 A.M. to 1:00 P.M., and from 3:00 P.M. to 7:00 P.M. When a pharmacy is closed, a notice must be affixed to the door to indicate the nearest pharmacy which is open.

PHARMACOPŒIAL SECTION OF THE PAN-AMERICAN MEDICAL ASSOCIATION.

BY LEWIS W. FETZGER, PH.D., M.D.*

In the past several years there have been a number of serious attempts to get up some enthusiasm on certain methods for rehabilitating the spirit of coöperation which prevailed between the medical and pharmaceutical fraternities in years gone by.

Last year a number of forward-looking leaders in pharmacy and medicine met during the Congress of the Pan-American Medical Association, in the city of Dallas, Texas, in an effort to bring about a frank expression of opinion as to the need and feasibility of a section devoted to drugs, with especial reference to the kinds which are in use in the North American and Latin American countries. This was done in the hope that by starting persons thinking about the matter there may be something actually accomplished in the perpetuation of an organization that may eventually be a permanent, and distinctly helpful, enterprise.

These discussions served to show how little attention had been paid to the relationship of the pharmacists' problems to those of the medical fraternity. Each profession made a cult out of its respective endeavors, and has treated it as a sacred and highly protected constituency. The discussions, to say the least, opened the way for a line of inquiry that would be most interesting and productive.

The gap between the medical and pharmaceutical professions is more a spurious one than real. When present, the gap is a very narrow one and shows itself chiefly in the attitude of mind due to a lack of a suitable vehicle for the interchange of thought.

The Pan-American Medical Association expresses the idea of the mutual relationship and the interdependence of the professions which aid medicine in pushing forward the boundaries for more exact knowledge. Its effort in that field is a give and take process in which any one of the participants may often receive quite as much as it gives.

Commensality will be the rule for the next Congress. It will be a "Floating Congress," aboard the S. S. Pennsylvania. The itinerary, requiring sixteen days, March 14 to 30, 1934, will include Havana, Colon, Cartagena, Puerto Cabello, La Guaira and San Juan. The idea is novel in many respects, and it is reciprocal in that it brings the Congress to the very doorsteps of our Latin-American brethren.

This represents the finest type of correlation, and we need have no fear of the outcome.

Theodore J. Bradley was in charge of the Section on Pharmacopœias at the Dallas meeting.

* Chairman, Section on Pharmacopœias, Pan-American Medical Association.

THE DEPARTMENT OF THE AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY

C. B. JORDAN—CHAIRMAN OF EXECUTIVE COMMITTEE, A. A. C. P., EDITOR OF THIS DEPARTMENT.

Editor's Note: The following paper by Prof. Edward P. Claus presents a method of teaching microscopical pharmacognosy that will make a subject that, to some, is dry, uninteresting and impractical, become interesting, instructive and enjoyable. I am fully aware of the fact that botanists will not agree with me that microscopical pharmacognosy may be what I have implied, but personal experience tinges my views. I am also aware of the fact that I have no authority to criticize the teaching of subjects outside of my field, but if all students, including those that may have special interest for the subject, must take certain courses, then it is our duty to make them as interesting as possible. A dry subject may become intensely interesting in the hands of a good teacher and a live one may lose all interest in the hands of a poor teacher. The paper by Prof. Claus will be helpful to teachers of pharmacognosy.—C. B. JORDAN, *Editor*.

MICROSCOPICAL PHARMACOGNOSY.

BY EDWARD P. CLAUS.*

Dr. L. K. Darbaker has not given me his original paper on this subject, but since his ideas embody our teaching plan, I shall try to relay to you some of his thoughts.

In the Pittsburgh College of Pharmacy, School of Pharmacy, University of Pittsburgh, the student in the freshman year studies biology, in the second year microscopy and in the third year, histological pharmacognosy. He has a distinct advantage in these studies by performing practical work in the same laboratory for these subjects under the guidance of the same group of instructors. The work has been correlated in such a manner that one course is related directly to the next.

The members of our department feel that when the average student enters college, in no matter which field, he is more or less ill at ease, nervous and easily discouraged due to the extreme change in environment. In consideration of these factors, we believe that the best method of beginning instruction in biology is the laboratory study of plant specimens with which the student is familiar, particularly, members of the spermatophytes which he sees practically every day. This procedure is in direct contrast to the usual method of study from the taxonomical viewpoint, from the lowest to the highest forms. However, we feel that, given something he can identify and examine easily, the student's first few days are made more pleasant, and his attention and interest are stimulated. A field aster, a morning glory flower, bean seedlings and corn seedlings, for the first few laboratory hours, followed by more complex spermatophyte forms, then members of the pteridophytes, bryophytes and thallophytes, interspersed with simple experiments on growing plants constitute the first semester's work. Living material is used whenever possible. Microscopical work is not considered except if important structures or tissues are to be seen, and then the microscopical slides are under the direct supervision of the instructor in charge. During the freshman year, the student is directed in the proper method of collecting, drying and mounting of botanical speci-

* Bacteriology and Pharmacognosy, School of Pharmacy, University of Pittsburgh.

mens, particularly of plant drugs, is encouraged to start an herbarium, and is given opportunity to enlarge this collection throughout his school career. Last year a number of our students displayed such mounts of medicinal plants in drug store windows during pharmacy week. The second half of the biology course is devoted to zoölogy in the same anatomical manner, from the higher, more familiar forms to the lower forms, macroscopic work only being considered. Field work, museum trips and trips to the medicinal plant garden are essential parts of the biology course.

The second year microscopy work first considers the microscopical animals, completing the zoölogy course, and then microscopical plants, of the algæ and fungi groups. Hence, this particular part of the work might be termed microbiology, with the exception that bacteriology proper is not touched upon in laboratory until the student's senior year. After the student has completed the microscopical botany course, observing single-celled plants as gleocapsa, pleurococcus and the like, the next natural step is the simplest cell of the higher plants, the parenchyma cell. This relationship is stressed, comparisons being made in the manner of structure, functions, reproduction, etc. From this point on through, the sophomore year might be termed elementary histological pharmacognosy, since in each laboratory period, the student learns of new cells and tissues, and of official plant drugs in which these cells and tissues are found. Instruction is given in the preparing, sectioning, staining and mounting of plant drugs. A study of starches, crystals, cell contents and fibrovascular bundles is also considered.

The third year histological pharmacognosy course enables the student to study how the various combinations of cells and tissues constitute the various plant parts. He studies the official plant drugs in groups: *i. e.*, barks, woods, roots, rhizomes, leaves, flowers, seeds, fruits, etc. Then, since he has a thorough knowledge of each individual cell, he can readily identify the plant part and tissues present in, for instance, a section of Apocynum cannabinum or in a powder of the same drug. Also he can identify powdered drugs and upon examination of a powder, he can state whether it is adulterated or not by the mere presence of a number of cells foreign to the plant part in question. His microchemical tests would enable him in some cases to name the adulterant. Since such products as talcum powders, artificial foods, infant foods, spices and condiments are commonly sold in the retail pharmacy, microscopical examination and microchemical tests for these products form an important part of the student's training.

All of the laboratory work is supplemented with lectures, recitations, displays, lantern slides, motion pictures and demonstrations as well as field work. By means of this orderly arrangement and obvious relationship of courses, we are convinced that the average student is encouraged to do better work, and is able to grasp the subject matter more easily and in a more coördinated form.

SHALL THE RELATIONSHIP OF BOTANY TO PHARMACOGNOSY BE MAINTAINED?

BY C. W. BALLARD, PHAR.D., PH.D.*

Editor's Note: The old question as to whether basic subjects should be taught by men trained in pharmacy is presented by Dr. Ballard in so far as it applies to botany. His arguments

* New York College of Pharmacy, Columbia University.

are excellent and no one will gainsay that it is not better to have these subjects taught by men trained in pharmacy *provided* they are specialists in their fields. Such teachers can make the application to pharmacy much better than can a teacher who is not so trained. However, we must recognize the fact that it is exceedingly difficult to secure well-trained specialists in general subjects who are also well trained in the professional subjects that are based upon them. Dr. Ballard's paper is worthy of careful reading by all interested in teaching pharmacognosy.—C. B. JORDAN, *Editor*.

The procedure of the current Pharmaceutical Syllabus in its division of subjects into basic and professional groups is excellent. However, owing to the close relationships between botany and phamacognosy, it is unfortunate that the content of the basic botany is not definitely stated. The subject matter of pharmaceutical botany in previous editions was manifestly too restricted to give the student a general knowledge of plants but it was a clear-cut statement of what the pharmacy student should have covered in his course. It diminished the difficulties of drawing a line of demarcation between botany and pharmacognosy as regards content.

The policy of extreme generalization is just as objectionable as that of specialization in planning any professional curriculum. This is especially true in pharmaceutical education because of the varied nature of the subjects included in the course. It is entirely possible in a university maintaining schools or divisions of business, chemistry, medicine, botany and the usual academic or collegiate courses to cover all the subjects of the outlined pharmacy curriculum, with the exceptions of pharmacy and pharmacognosy. Economic conditions are perhaps increasing the frequency of this procedure. It is desirable that purely academic subjects as English, languages and mathematics be taught by those qualified in these branches and not by pharmacy school instructors. However, in subjects of the science group it is desirable that the instructor consider both the general aspects of the subject and its relations to pharmacy. In this manner we can better further the claims of pharmacy as a vocation requiring a thoroughly integrated course of professional education.

The advisability of securing contact between botany as a basic subject and its specialization, pharmacognosy, has been frequently commented upon. The general tenor of these comments is reiterated in a paper, "The Teaching of Pharmacognosy," by Prof. Bacon (JOUR. A. PH. A., Nov. 1930), in which the following statements occur. "The nature of the botany courses offered to pharmacy students should be carefully considered . . . . pharmacy students as well as students of other schools should be given in their first courses sound, working fundamentals . . . . to serve as a basis in specialized study." That this advisability of a proper coördination between basic and professional work applies equally well in other subjects, is evidenced by the following quotations from the current syllabus:

Page 32 (Applied Bacteriology): "When laboratory courses in Bacteriology are given to pharmacy students in medical, biologic or other departments, the attention of instructors should be called to the specific pharmaceutical applications listed below."

Page 51 (Inorganic Pharmaceutical Chemistry): "Experience has proven that it is unwise to rely too much upon an understanding of subjects previously studied."

Page 128 (Pharmacognosy): "Terms which students have supposedly learned in botany are not repeated but these terms should be used and applied."

I am not unmindful that the adoption of the blanket statement "standard college grade" for botany presents the following possible advantages—it checks tendencies to narrow the botanical teaching to those portions applicable to pharmacognosy, thus limiting its general educational features; it favors a mingling of the pharmacy men and the students of other schools; it relieves the pharmacy school of the labor and expense of a division of botany; it is a convenience in schools where the bulk of the general education is segregated as a pre-pharmacy year; it facilitates transfer of students to or from a pharmacy school to other schools of a university. But against all these possible advantages is the question of what constitutes standard college grade, particularly in botany, and the interpretations which individuals and colleges may place upon this term. A statement of hours does not remedy the situation. There is probably a greater diversity of opinion as regards content of the courses in the botanical subjects than there is in pharmacy and chemistry. Hence, there is a greater necessity for definite statements as to the content of the botany course. Furthermore, the statement in the Syllabus of the reason for the omission of syllabi for the basic subjects is perhaps the strongest argument for their inclusion. If the emphasis on integral parts of a given basic subject varies so appreciably in different colleges, it would appear advisable to establish some guide as to where, in the opinion of pharmaceutical educators, the emphasis should be placed. Notwithstanding the general statement that basic subjects are not applied, I hardly think there will be a difference of opinion among us as to the applications of botany in the teaching of pharmacognosy.

Failure on the part of the teachers in pharmacy colleges to at least attempt to influence the trends of teaching in the basic subjects may be construed as due to lack of necessity, lack of interest or, what is worse for pharmaceutical education, incompetency and I do not believe that these conditions prevail. Formerly in many instances, the instruction in botany and pharmacognosy in the pharmacy school was given by men whose sole botanical training was received in the pharmacy course. Frequently this specialization, together with lack of time, resulted in a restriction of the course in botany to its strictly pharmaceutical applications. At present, in a goodly number of schools, pharmacognosy and botany are taught by men who have not only been pharmaceutically trained but in addition have studied botany in other institutions and in some instances have majored in this subject for an academic degree. Their viewpoint is broadened and they are as capable of teaching general botanical science as the instructor in an academic college. I believe that these men can outline a course in botany which will be acceptable to our universities as of standard college grade and which will serve as a better foundation for pharmacognosy than the usual academic course.

The construction of a syllabus in botany to meet our requirements, both general and specialized, offers no serious difficulty. Undoubtedly each of us would find that the introductory course in botany in our respective universities is considered a course of standard college grade. With this as a working basis, the planning of a course to maintain the integrity of botany as a basic or cultural subject and at the same time place the proper emphasis on its relations to pharmacognosy, is entirely feasible. The syllabus for botany submitted by Prof. H. R. Totten in the preliminary draft of the present Syllabus, is an excellent example of the coördinating of botany with pharmacognosy without sacrificing the interests of either. In our

university class, for the past eight years, we have been giving a course along similar lines. The basis for our course is Botany 1–2 of Columbia College in an amplified and supplemented form to better meet our needs as a preparation for pharmacognosy. Pharmacy men who subsequently enter other schools in the university receive 6 points of credit for the botany of the pharmacy school. The time allotted is 240 hours, 96 didactic and 144 laboratory.

Our foundation course in botany must also be considered as related to microscopic pharmacognosy and here the desirability of correlation is even greater than in macroscopic pharmacognosy. Many of the academic courses in botany very properly present the topics of cellular structure and cell contents merely as incidental factors in plant organization and function. This plan fits the needs of the college freshman rather than those of the pharmacy student as the former may or may not apply his knowledge of botany in subsequent work, whereas the pharmacy man must do so in pharmacognosy. Where school organization compels a separation of botany and pharmacognosy, the content of the latter course must be increased and duplication is almost unavoidable. The difficulties of maintaining correlation between separated courses are known to all teachers. If the student receives part of the instruction on fibres, trichomes and starch grains in the botany course and another part in pharmacognosy, it is more than likely that duplication will be necessary. The instructor in pharmacognosy must review the previous work or rest under the uncertainty as to how well it has been retained by members of a class. His uncertainty is materially increased if the teaching in botany is without specification as to content.

It is to be regretted that microscopic pharmacognosy has been classed as an optional subject. The legal standards for drugs require familiarity with the microscopic as well as the macroscopic characters. In the pharmacy curriculum the purpose of our instruction in pharmacognosy is to enable the pharmacist to intelligently read the official descriptions. Giving microscopic pharmacognosy a secondary classification not only permits the elimination of a necessary professional subject but one which gives promise of ready recognition in academic botanical circles.

We are all familiar with the tendency on the part of other educational institutions to minimize the work of the pharmacy college. Of all the subjects in our curriculum, pharmacognosy is perhaps the one upon which we can rest our strongest claims for academic recognition. It is a type of work which is not duplicated in any other part of a university. Its scope and research angles are sufficiently broad as to warrant it being included with graduate courses in the division of botany in any university. To further this recognition we must assume responsibility for the botanical courses which are the foundation for pharmacognosy. We must not concede that an introductory course in botany without qualification as to content, constitutes an adequate preparation for pharmacognosy.

COLLEGE OF PHARMACY,
COLUMBIA UNIVERSITY.

Hungary.—Pharmacies must always be open to the public. An edict of 1919 fixes the opening hours from 8:00 A.M. to 7:00 P.M. For night service, Sundays, holidays, the authorities arrange a rota with the pharmacists for opening from 1:00 P.M.

RELATION OF CAFFEINE AND COFFEE TO HUMAN EFFICIENCY.*

BY RALPH HOLT CHENEY.

Efficiency and diet occupy a more prominent position in the public mind to-day than in all previous history. At the moment, caffeine beverages, especially coffee, are lauded or berated vigorously regarding their value in the diet in relation to human efficiency.

Based upon "whims and guesses," coffee has been praised or condemned for centuries. What is the scientific evidence "pro" and "con?" Historically, we find a prohibition edict by Khaine Beg, Governor of Mecca in 1511, who started a campaign which condemned coffee as an inebriating beverage forbidden by the Koran because the people frequented coffee houses rather than the mosques. Coffee and coffee houses were taxed by European governments as a source of revenue. Later, coffee houses were prohibited by Charles II of England as "Seminaries of Sedition." Coffee houses have served as gathering places for public discussions of governmental affairs. They were the predecessors of the boulevard cafés of Paris and the coffee-house taverns of England. This English prototype appeared in the United States where the coffee houses of Boston and New York harbored the instigators of the Boston Tea Party and revolutionary propaganda.

In spite of six hundred years of agitation associated with coffee, its consumption has increased constantly from an insignificant amount to three billion pounds annually, and its use has spread from the Abyssinian hillsides to world-wide consumption. Mocha coffee from the original home of the plant now supplies less than 3% of the seeds (coffee beans) of this sweet-pulped, cherry-like fruit which was introduced in America in 1717. Its cultivation has changed the economic map of several countries. Brazil has two billion coffee trees, Colombia a quarter billion, and the success or failure of the crop is the chief factor in the economic situation in these countries. Eighty per cent of the total gold value of Salvadorean exports is coffee. Although the plant is foreign to American soil, no better coffee is marketed to-day than the Colombian or Brazilian Santos from the Uplands where it is prepared by the most modern methods.

The United States consumes over one-half of all the coffee exported from the cultivated areas. New York City requirements annually total seventy million pounds, for which we pay thirty million dollars. Space limitation causes me to refer you to a book, "Coffee" (1), published by the New York University Press, for botanical characteristics; and also, for further details of the interesting, romantic history and economics of the plant and its beverage.

Undoubtedly, more scientific experimentation on the subject of caffeine and coffee effects has been conducted during the last twenty-five years than in all previous time. The results of such investigations are the only justifiable bases from which we may make our deductions regarding the physiological effects of the coffee as such, and of its individual ingredients.

Many investigators have reported that caffeine and caffeine beverages are undesirable for young children, neurotics, sufferers from severe arteriosclerosis, gastric hyperacidity, and other abnormal conditions. Likewise, the administration of caffeine for therapeutic purposes, such as stimulation of the coronary circulation in cardiac deficiency, are well known. May I make it perfectly clear, however, that the data presented in this paper is not concerned with the allergic effects of caffeine nor of the coffee beverage upon pathological conditions. This paper does not deal with its therapeutic value. All statements and figures refer entirely to *normal* physiology. The experimental animals and human subjects employed in the investigations were selected purposely from individuals of as nearly average good health as could be determined readily. In the caffeine work, the Merck product was used, and in the coffee work, the beverage was prepared by a rapid method (drip or vacuum) from recently torrified Colombian and Brazilian, high-grade beans.

Isotonic and isometric records of striated muscle fatigue curves of homologous muscles were made under non-treated and caffeine-treated conditions. The method and period of treatment were maintained uniformly throughout the series. Detailed discussions may be found in the writer's earlier papers, especially on the animal gastrocnemius behavior (2, 3).

Although Herxheimer (4) found that caffeine was of no benefit to the athelete, and P. T. Osborne states that caffeine actually interferes with the best muscular effects, the experimental data in this paper are more in agreement with H. C. Wood, Jr., (5) and others whose results offer definite evidence of improved muscular function.

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* New York Branch, A. PH. A.—See page 70, January JOURNAL.

An extended series indicated that better physiological coördination of the motor mechanism was obtained in the striated muscle action of the frog under the influence of low concentration of caffeine. According to the data presented in the August 1932, issue of the *Journal of Pharmacology and Experimental Therapeutics*, the optimum dosage (3) for these muscles for delaying fatigue was 0.1 mg. per Gm. body weight. Similar studies using the coffee beverage as such, in lieu of the purified caffeine, showed a parallel response for the gastrocnemius muscle.

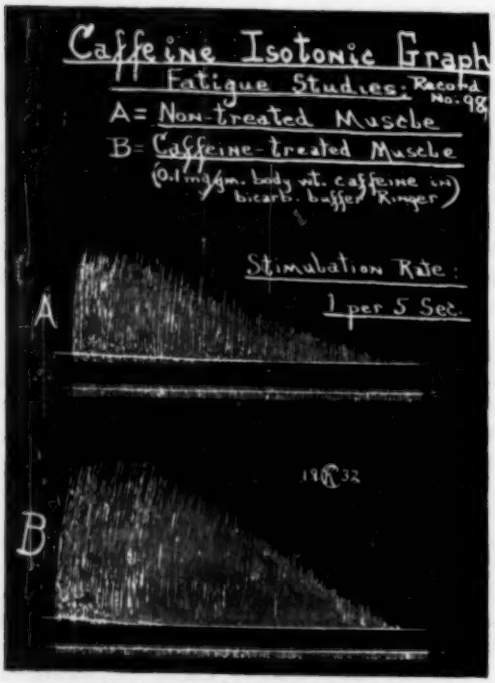

Fig. 1.—Caffeine isotonic graph.

A mathematical analysis of these fatigue curves in computing the XY values (Time *to* one-half fatigue × Height *at* one-half fatigue) demonstrated a greater XY value in both the caffeine and coffee curves as compared with the normal, non-treated result.

Under uniformly controlled circumstances, a study of the physical fatigue in human male subjects was attempted. The variable factor was the treatment; namely, the consumption of equal volumes of hot water, black coffee, or hot water plus caffeine (equivalent to the amount in the coffee) prior to the fatigue test involving a weight-lifting exercise every ten seconds to complete fatigue. Additional non-treated, starch capsule plus hot water, or plain hot water days were completed in order to correct for any practice, accommodation or experience factor which may have developed during the experimental tests. The Work Done was computed by the simple formula: WD = Weight (Gm.) × Height lifted (cm.) × Number of lifts. The result in gram-centimeters showed a sequence of an increasing amount of Work Done in the order of the non-treated or hot water day (least), coffee day, caffeine day (most). Attention was given primarily to the following physiological factors:

1. Blood-pressure variations: Systolic and diastolic.
2. Respiration: Rate and depth by pneumographic record.
3. Time required for a complete recovery of all factors after fatigue.

As compared with the non-treated fatigue values, the blood pressure and pulse variations were negligible; that is, their variation under the treated conditions was similar to their variation under the non-treated conditions. The increased respiratory rate and depth in the coffee instance indicated an increased oxygen consumption.

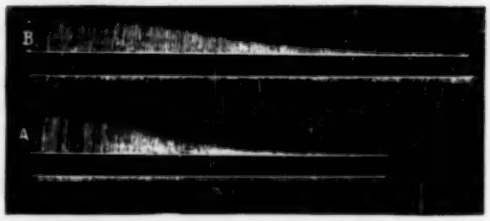

Fig. 2.—Caffeine isometric graph.

Fatigue Studies: Record No. 888.
A = *Non-treated* muscle; B = *Caffeine-treated* muscle. (0.1 mg./Gm. body weight caffeine in bicarb. buffer-Ringer) stimulation rate: 1 per 5 sec.

Several years ago (6), I conducted a series of tests to determine blood-pressure variations *without fatigue*, as influenced by caffeine and by coffee in comparison with normal behavior. This work has been repeated recently as an additional series. Similar and additional substantiating data were obtained. The accompanying graph separates the primary and secondary coffee effects

and indicates the fact that other substances are involved besides caffeine in the total coffee effects. Note that the caffeine or coffee increased the blood pressure only a few millimeters in excess of the ordinary luncheon (food) effect.

Although caffeine has been reported as a vaso-dilator of cerebral vessels, investigations (7) by Dr. P. G. Denker of Bellevue Hospital, caused him to conclude that caffeine definitely lowers the cerebrospinal pressure for half an hour. This fact is suggested by some workers as a possible explanation of the recognized relief induced by coffee in instances of mild hypertensive or nervous headaches, cerebral concussion, fractured skull and brain tumor. Sollman and Pilcher (8) reported in 1911 that caffeine causes vaso-dilation of the cerebral vessels. Wiechowski (9) had reported similar results in 1902 and claimed the dilation was due to a direct decrease in the tonus of the intracranial vessels. Such action with a rigid cranium would force out the cerebrospinal fluid and increase its pressure. Denker obtained the reverse results. With reference to the decreased cerebrospinal pressure it is significant that caffeine diuresis through glomerular action, involves primarily only an increase in the water content of the urine. This water loss must be lost necessarily from the body tissues through the lymph and blood. It must accomplish

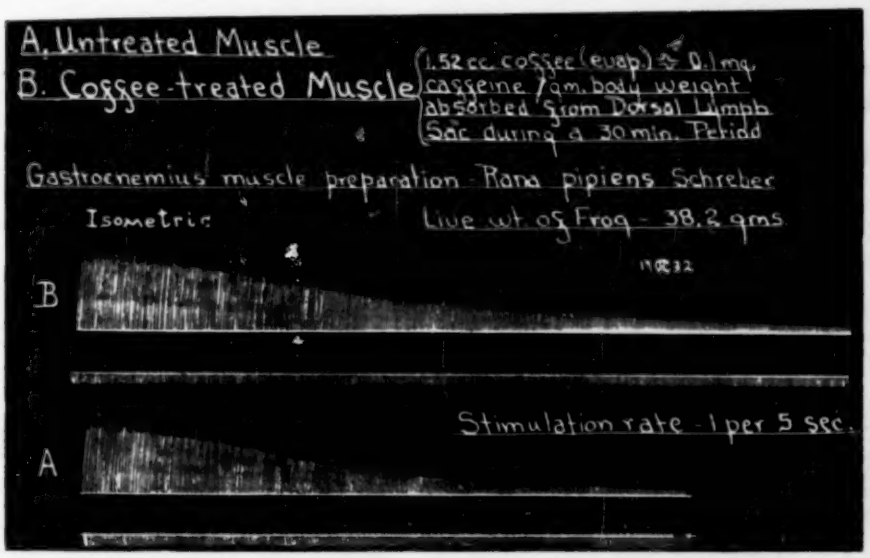
A. Untreated Muscle
B. Cossee-treated Muscle
1.52 cc. cossee (evap) = 0.1 mg. caffeine / gm. body weight absorbed from Dorsal Lymph Sac during a 30 min. Period
Gastrocnemius muscle preparation Rana pipiens Schreber
Isometric
Live wt. of Frog - 38.2 gms
B
Stimulation rate - 1 per 5 sec.
A

Fig. 3.—Coffee effect on muscular fatigue.

automatically, a reduction in brain volume with a consequent decrease in cerebrospinal fluid pressure.

The increased respiratory rate and depth, referred to earlier in connection with the fatigue as influenced by caffeine and coffee, is related also to an intercranial pressure. In 1913, Dixon and Halliburton (10) noted that reduction of carbon dioxide in the blood decreases the rate of cerebrospinal fluid secretion. Therefore, respiratory stimulation by caffeine or coffee, resulting in increased rate of carbon dioxide ventilation from the lungs, would decrease the rate of cerebrospinal fluid secretion. Apparently, caffeine lowers intracranial pressure by means of its combined pharmacologic actions rather than by any specific, single effect.

Dr. A. L. Winsor (11) of Cornell University, reported last October that coffee increases the salivary secretions in volume per unit of time. Such stimulation automatically improves digestion by making a greater enzymic mass available.

Professor Hollingworth's experimental series (12, 13) on the mental effects of caffeine and coffee are the best available studies on this phase of the subject. He reports a clearly distinguishable mental stimulation as evidenced by greater accuracy in the performance of work done.

Recently at Long Island University, a simplified psychodometer was devised to measure the reaction time in man with a visual-mental-physical coördination test. Quantitative data on

the relationship of caffeine and coffee separately to the normal reaction time were compiled. The subject was required to recognize a visual stimulus (light color), interpret it, and perform a muscular act in accordance with the color of the particular stimulus involved. Caffeine and coffee were each more effective in reducing the total reaction time in women than in men. The sequence in both sexes was as follows:

1. Non-treated tests required the longest reaction time.
2. Coffee—intermediate.
3. Caffeine-treated tests required the shortest reaction time.

In various physiological effects studied regarding muscular action, fatigue delay, respiration, pulse and mental effects, the sequence of minimum to maximum physiological stimulation is generally non-treated, coffee-treated, caffeine-treated. The absence of injurious effects in the majority of cases suggests the importance of optimum consumption. Excessive stimulation can be produced, but was not apparent in the amounts administered in the experiments upon normal animals and man, although the quantities given were in excess of average consumption. The absence of after-effects and accumulative effects is associated doubtlessly with the two primary facts:

1. Caffeine is combined with other chemical substances in coffee.
2. Caffeine itself loses CH_3 groups in the body and is excreted within a few hours in the urine as mono- and dimethyl xanthine.

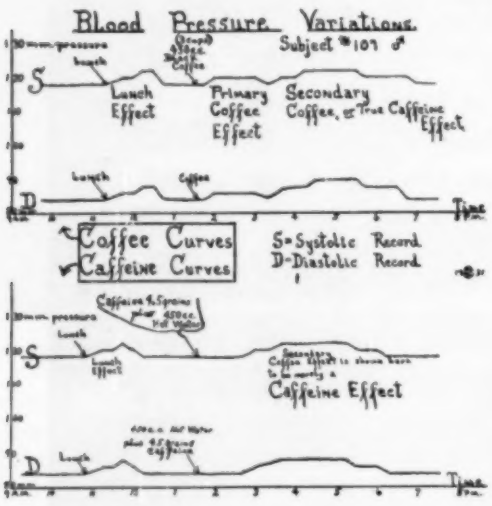

Fig. 4.—Blood-pressure variations: caffeine *vs.* coffee effects.

Likewise, Gutman (14), in agreement with this conception, observed that caffeine and coffee effects are not the same in abnormal persons (patients) showing allergic manifestations to coffee. Whereas caffeine may cause definite physiological disturbances, coffee may be well tolerated. Moreover, the action of coffee is not due solely to caffeine, but to the many compounds organized during the roasting process, and which are present in both decaffeinated and ordinary coffees.

Caffeine and coffee increase blood pressure very few millimeters, respiration and oxygen consumption slightly, and stimulates the brain and other parts of the central nervous system. These stimulants also delay fatigue and lower the cerebrospinal pressure. Caffeine is less effective in the coffee beverage than separately. Neither complex, caffeine nor the coffee beverage as such, can replace nutritive metabolism in the normal health of the tissues. It has been reported that both complexes increase basal metabolism; hence, food should always be taken regularly at the customary periods if the reserve forces of the body, which are reduced by increased metabolism, are to be replenished properly. Nevertheless, many people labor under the misconception that coffee has the ability to replace food merely because its stimulating action persists for several hours after consumption. It is an aid to functional efficiency, not a substitute for body fuel.

The variations from the normal due to coffee stimulation are slight and, in the reasonable amounts consumed ordinarily, are far below the maximum physiological disturbances, for the correction of which the body is equipped by nature to adjust itself without injurious effects.

Apparently, the delicate correlation between the increased blood flow and the increased respiratory rate accomplishes, in a fortunate sequence, *both* the more rapid removal of fatigue products from the body tissues to the blood; and, the greater purification (oxidation) of the blood

volume per unit time in the lungs. Fatigue, due to the accumulation of waste products in the tissues, is correspondingly delayed. Caffeine separately or in the coffee beverage, stimulates the circulation and respiration. The increased activity of one of these systems without a parallel response by the other, would be injurious. The stimulation of both synchronously, produces or "sets" the body metabolism at a higher level of physiological efficiency. That the body readily adjusts itself to the level of performance without injury is evidenced by the fact that the recovery time of the fatigue is practically identical with conditions subsequent to normal fatigue.

The bulk of available experimental data seems to indicate that the majority of the population may take advantage of this beneficial aid to body metabolism. Every debatable question has its "pro" and "con." Each of us has a caffeine and coffee tolerance which must be determined individually, and our consumption governed accordingly.

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HOSPITAL SALES EXEMPTED FROM CODE RESTRICTIONS.

Hugh S. Johnson, Administrator for Industrial Recovery, has issued the following order effective from February 2nd:

"Pursuant to authority delegated to me by executive orders of the President, including Executive Order No. 6543-A, dated December 30, 1933, it is hereby ordered that those members of industries subject to codes of fair competition who sell or may sell supplies or materials to hospitals of the United States which are supported by public subscription or endowment, and not operated for profit, within the limitations hereinafter provided, be and they are hereby exempted from compliance with provisions of such codes governing sales; provided, however, that the exemption hereby granted shall be limited to and operative only in connection with such sales made by such members to such institutions; that nothing in this order contained shall relieve any such member at any time from the duty of complying with all other provisions of such codes; and that this order shall not become effective for a period of ten days in order that consideration may be given to the objections, if any, of interested parties thereto. At the expiration of such period this order shall become effective unless I, by my further order, otherwise determine."

PROCEEDINGS OF THE LOCAL BRANCHES

"All papers presented to the Association and Branches shall become the property of the Association with the understanding that they are not to be published in any other publication prior to their publication in those of the Association, except with the consent of the Council." —Part of Chapter VI, Article VI of the By-Laws.

ARTICLE III of Chapter VII reads: "The objects and aims of local branches of this Association shall be the same as set forth in ARTICLE I of the Constitution of this body, *and the acts of local branches shall in no way commit or bind this Association, and can only serve as recommendations to it.* And no local branch shall enact any article of Constitution or By-Law to conflict with the Constitution or By-Laws of this Association."

ARTICLE IV of Chapter VII reads: "Each local branch having not less than 50 dues-paid members of the Association, holding not less than six meetings annually with an attendance of not less than 9 members at each meeting, and the proceedings of which shall have been submitted to the JOURNAL for publication, may elect one representative to the House of Delegates."

Reports of the meeting of the Local Branches shall be mailed to the Editor on the day following the meeting, if possible. Minutes should be typewritten with wide spaces between the lines. Care should be taken to give proper names correctly and manuscript should be signed by the reporter.

CHICAGO.

The monthly meeting of the Chicago Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held January 16, 1934, at the University of Illinois College of Medicine.

President Terry opened the meeting and called for the report of the nominating committee for officers of the Branch for the ensuing year. Dean Day, chairman of the committee, presented the following nominations:

President, G. L. Webster
First Vice-President, S. W. Morrison
Second Vice-President, R. A. G. Linke
Third Vice-President, H. M. Emig
Secretary-Treasurer, L. Templeton
Delegate to the House of Delegates, R. E. Terry.
Committee Chairmen:

Membership, Thomas P. Rylands; Legislation, J. Riemenschneider; Practice, I. A. Becker; Medical Relations, Dr. Bernard Fantus; Publicity, A. E. Ormes.

By a unanimous vote the nominees were declared elected.

Secretary-Treasurer L. Templeton was called upon to give a financial report of the past year. The report showed a balance of $1.15 in the treasury.

Dr. Muehlberger, chemist for the County Coroner, was introduced as the speaker of the evening. His subject was "The Toxicology of Common Drugs." He stated that due to the nature of his position he was experienced primarily with fatal poisonings. A summary was made of the types of fatal poisonings that he was called upon to investigate, such as accidental, suicidal or with criminal intent. Mention was made that fashions were found in suicides due to the publicity that follows in the newspapers.

Common poisons and their detection by (1) odor, (2) chemical analysis, (3) biological analysis, (4) quantitative analysis, were discussed at some length. There must be proof beyond doubt for criminal court procedure.

Dr. Muehlberger pointed out that quantitative results were very hard to obtain in the case of mercury or arsenic poisoning due to the fact that the organic preparations of these two elements will show large amounts of the element in the body, which means nothing so far as a fatal dose is concerned.

Lye, as found in sink and drain cleaners, was mentioned as being one of the worst poisons to combat, as scar tissue is produced that fails to heal quickly. The lye seems to eat deeper into the tissues as time goes on. The acids do not produce an insidious scar tissue.

Dr. Muehlberger stated that he had not used Methylene Blue as an antidote for cyanide or carbon monoxide poisoning, but had read much of the literature that was being published lately regarding its use. He had found amyl nitrite, sodium nitrite and sodium thiosulphate to be beneficial in the treatment of these poisonings.

The discussion was followed with an open question and answer period which was thoroughly enjoyed by the large group assembled.

The meeting was closed by the newly elected president, G. L. Webster.

L. TEMPLETON, *Secretary.*

NEW YORK.

The January meeting of the New York Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held on January 8, 1934, in the College of Pharmacy, Columbia University. President Bilhuber was in the chair and about fifty-five members and guests attended.

The report of the secretary was read and accepted. Following this, Mr. Currens, treasurer, reported.

Chairman Lehman, of the Committee on Legislation and Education, reported that the State Board of Pharmacy was gathering samples in cosmetic shops to see if their drug products met Pharmacopœial requirements.

Chairman Kidder, of the Professional Relations Committee, reported that the Physicians' and Pharmacists' Dinner Committee was still functioning. Dr. Wimmer reported a physicians' and pharmacists' meeting to be held by the Academy of Pharmacy in February. Dr. Ballard called attention to the meeting of the Bronx County Medical Society on January 17th, for which a display of U. S. P. and N. F. preparations was being arranged.

The chairman of the Membership Committee, Dr. Kassner, reported applications for Branch membership from Frank Pokorny, John Torigian and Richard G. Keller. All were voted to membership in the Branch.

Chairman Lehman, of the Nominating Committee, reported the following nominations for Branch officers during 1934:

President, Charles W. Ballard
Vice-President, Frederick C. A. Schaefer
Treasurer, Turner F. Currens
Secretary, Rudolf C. Hauck
Chairmen of Committees:
Audit, Ernst A. Bilhuber
Professional Relations, Herbert C. Kassner
Legislation & Education, Robert S. Lehman
Progress of Pharmacy, Morris Dauer
Membership, George J. Simpson
Secretary Remington Medal Committee and Delegate to House of Delegates, Hugo H. Schaefer.

Mr. Lehman also reported that the Nominating Committee recommended that the chairmen of the respective committees should appoint members who could report at the meetings, should the chairman find it impossible to attend.

On a motion made by Dr. Schaefer and duly seconded by Dr. Kidder the secretary was requested to cast one ballot electing the new officers unanimously. Dr. Schaefer included in his motion the recommendation of the Nominating Committee pertaining to appointed members for the several committees.

Following the election of officers Dr. Bilhuber thanked the members of the Branch for their coöperation and turned the meeting over to President Ballard. The new president expressed his appreciation to the Branch for the honor bestowed upon him and proceeded to briefly outline plans for future meetings.

After some brief introductory remarks, Dr. Ballard presented the first speaker of the evening: Mr. James F. Hoge who spoke on the Tugwell Bill, the Black Bill and the Copeland Bill. Mr. Hoge's discussion was from the viewpoint of the lawyer. Brief abstracts of his comprehensive address follow. It will be understood that it is difficult to do justice to the speakers, whose well-prepared addresses are based on careful studies of the legislation.

FOOD AND DRUG LEGISLATION.

ABSTRACT OF AN ADDRESS BY JAMES F. HOGE OF THE NEW YORK BAR.

Mr. Hoge introduced his remarks by stating that the food and drugs legislation involved the question as to whether the legislation shall be by Congress, an enforcement by the courts, as now, or legislation and enforcement by a government officer in the Department of Agriculture.

The speaker outlined some of the activities of the present drug law which was enacted in 1906. He stated that dissatisfaction with the present law is usually asserted in four principle respects. *First*, to establish a violation of the law the Government must prove that statements regarding curative effects of drugs are not only false but are also fraudulent. He said that there is reasonable argument for the suggestion that the Government should be relieved of the burden, and added that where an honest mistake is made through error or inadvertence it seems harsh to inflict criminal punishment, but the public health is involved. *Second*, criticism of the existing law is, that it does not apply to advertising. *Third*, the present law does not apply to cosmetics. *Fourth*, the general complaint is that the law needs improvement in definitions and administrative detail.

He referred to the fact that the Tugwell bill as first formulated would vest in the

Secretary of Agriculture broad and almost unsupervised legislative, executive and judicial powers. Mr. Hoge spoke at length regarding the latter provision in discussing the Copeland bill.

The speaker gave a history of the various bills which have been introduced and analyzed, the Copeland draft, which he said evidenced that criticisms made of the Tugwell bill were valid. In his opinion, the Copeland bill shows the sincerity, fairness and intelligence of the Senator. This proposed legislation is a revision of the Tugwell bill which it follows section by section and in some sections its language is retained; the speaker gave a careful analysis of the draft and an explanation of the changes which have been made.

He stated that the general administrative provisions of the Tugwell bill have been deleted and in their place a new section has been inserted which authorizes the secretary to promulgate regulations with the aid and advice of a committee on Foods and a committee on Drugs, each to consist of five members appointed by the President of the United States. The bill provides for court review of regulations vesting the courts with jurisdiction to restrain by injunction enforcement of any regulation shown to be unreasonable and not in accordance with law or that will cause the petitioner substantial damage by reason of this enforcement.

After further discussing the Copeland legislation the speaker analyzed the bill in the House of Representatives by Congressman Black which carries in its provisions the amendments suggested by James H. Beal. He said that to accomplish the objectives it is largely a matter of choice whether the new bill is enacted or the present law amended. For amending the law the bill by Congressman Black will accomplish the purpose and Senator Copeland's measure will do so in an entirely new law. Neither of these bills are subject to the criticisms and valid objections which were made to the Tugwell bill.

The speaker discussed the power of seizure vested in the Secretary of Agriculture. The former bill modifies this power and the Copeland bill retains substantially the Tugwell provisions. He discussed at some length the advertising provisions and wording of labels. He said that speakers for the Tugwell bill referred frequently to the regulations being subject to review by the cou ts and violations of the prohibitions of the bill can be established by trial. He said this was neither theoretically nor practically true under the bill as drawn. He spoke at length regarding multiple seizures and the effects and referred to the fact that the Government has seized, for instance in New York, Pittsburgh, Philadelphia, Baltimore, Oakland, Calif., Portland, Me., Miami and elsewhere, simultaneously with the threat implied in the situation that if an adjustment of the controversy satisfactory to the Department is not promptly made more seizures will follow. The speaker gave a very complete explanation of the effect of such seizures. He said that as a legal matter and as proper law-making the seizures should be limited to adulterated poisons, putrid or filthy goods and misbranding should be punished by indictment and prosecution with a hearing at which the differences may be reconciled. He said, "it is conceivable that misbranding of a flagrant nature representing an article to be a cancer cure might be imminently dangerous to public health and the public should be protected." To protect the public against that and also to afford the defendant an opportunity to be heard a proceeding in equity by the Government for injunction would be appropriate. Provision for this is made in the Black bill and a simple amendment to the Copeland draft would make a similar provision.

The speaker concluded his remarks by saying that we should have legislation which will not violate American principles of law-making and law enforcement; a law that is fair to the public and to the people who try to do business with the public. The legislation should, as far as possible, stamp out fakes and frauds and he thought that such legislation could be had without discarding our legislative and judicial institutions, and both the Black and the Copeland bills are evidences of it.

The laws which contain blanks to be filled in by a bureau chief are open to definite possibilities of abuse. He stated that the advocates of the Tugwell bill had the protection of the public at heart, and referred to possibilities with the change of officials; their viewpoints may be radically different. Mr. Hoge concluded by saying: "In the final analysis, more than a food and drugs law is involved in this question. The objection is not primarily an objection to any particular legislation, but to an attitude of mind and the theories of immature idealogists upon which this legislation seems to be based. This attitude of

mind disdains the legislative and judicial machinery. I concede readily the existence of abuses, defects and miscarriages in our legislative and judicial institutions. As a lawyer I deplore them. But, I call all to witness that these institutions afford security and safeguards which are inherently necessary if this country is to remain free."

The second speaker for the evening was Mr. S. L. Mayham who spoke about the new food and drug legislation from the standpoint of the cosmetic industry. A brief abstract of his address follows:

Food and Drug Legislation from the Standpoint of the Cosmetic Industry.

ABSTRACT OF AN ADDRESS BY S. L. MAYHAM.

The speaker stated that the Tugwell bill had ceased to be of interest, having been replaced by the Copeland bill, S. 2000, and another bill by Congressman Black has been introduced. He said that the latter was formulated along the lines of the argument presented by Dr. James H. Beal at a hearing some time ago. He stated that Senator Copeland had failed to make certain changes in which the cosmetic industry is deeply interested. The first is a definition of the term "drug." The cosmetic industry is ready to accept regulation but does not want to have its products classified as drugs except where curative claims are made. Under the Copeland bill many of the cosmetic products are included. The industry also objects to certain definitions applied to an advertisement, being too broad. The advertising regulations include all representations of facts or opinion disseminated in any manner by any means. This would include house to house canvassers.

The speaker said the Copeland bill provides that the name and the place of business of the manufacturer, seller or distributor must appear on every package, but if all this information is necessary there are some packages on which the type of labels would have to be very small. He stated that if the definition for antiseptics is required, practically every preparation of that class would have to be provided with a new label. The cosmetic industry objects to the licensing provision in the Food and Drugs Act. Under publicity, the Copeland bill provides that information shall be disseminated regarding the dangers of certain cosmetics. There is a provision in this draft that no person who is a member of the Department of Agriculture or who has a financial interest in the manufacturers' advertising the sale of any food, drug or cosmetics shall be eligible to appointment on the committee provided by the law. The speaker contended that under its provisions scientists in the cosmetic and pharmaceutical fields could not serve on the committee, nor any of the technical advertisers serving in that capacity at the present time.

The cosmetic industry objects to the definition which includes all substances and preparations other than foods and all diseases to affect a structure or any function of the body of man or animals; also to the provision of the bill which considers cosmetics adulterated if they contain poisonous or deleterious ingredients, likely to be *imminently* dangerous to the user under the condition or use prescribed in the labeling. It is the opinion of the cosmetic industry that the word "imminently" could lead to a great amount of litigation.

The speaker stated that the industry had no fear of any trouble arising from restricting dangerous poisons or deleterious ingredients and are interested in seeing such legislation enacted. He considered that some changes in the Beal draft should be made. The cosmetic industry would prefer to be entirely divorced from the Food and Drugs Act. He favored a measure that is fair and satisfactorily protects alike the interests of the consumer and those of the manufacturer.

Dr. Wharton, of the local Department of Agriculture office, complimented both speakers on their fair and adequate discussion of the proposed legislation, and he expressed regret that Department policy made it impossible for him to take part in the discussion.

Dr. Fischelis called attention to the fact that the speakers actually brought forward some points in favor of the Tugwell bill. He also went on to explain that the power to regulate advertising should be vested in some competent authority. Advertising goes before a public not educated in law nor technical points, and many of these statements have a different lay interpretation which is not infrequently misleading. Dr. Fischelis also pointed out that greater flexibility was required in the law due to rapid changes which take place. He especially pointed out the need for controlling radio advertising which reaches so many people at once and so quickly. And finally he criticized the industry for not

admitting the inadequacy of the present law when the new was proposed.

Since there was no further discussion the meeting adjourned following a rising vote of thanks accorded all speakers.

RUDOLF O. HAUCK, *Secretary.*

NORTHERN NEW JERSEY.

The Northern New Jersey Branch, of the AMERICAN PHARMACEUTICAL ASSOCIATION, met for its first meeting of the new year on January 15th, in the main building of the Rutgers University College of Pharmacy.

After the reading of the minutes, President Little introduced two of our newest members, Albert Hawes and Milton Kahn, who were participating in their first meeting.

The Membership Committee then proposed the following individuals for inclusion on our roll: Ralph Nacca, James A. Bauman, William J. Ohland, Milton Jungling and George Mitterman. They were duly elected.

Plans are rapidly being consummated for the joint meetings between the physicians, dentists and the Branch. It is hoped that many pharmacists who are not members will attend these sessions and bring their medical and dental friends. Mr. Mecca, who is in charge of the programs, assures us that every minute will be taken up with topics and demonstrations of real interest.

Norman Silsby, the first speaker on the new series of 10-minute talks concerning some phase of the profession, read some of the absurd advertising claims made by a manufacturer relative to a product being detailed to physicians. He thus illustrated how the doctor is oftentimes made to accept and prescribe inferior medicines solely on the strength of falsely advertised virtues. "The pharmacist should work in closer coöperation with the physician," said Mr. Silsby, "and forestall these false prophets of therapeutics."

He also compared the cost of detailing to a pharmaceutical house with personal visitations by pharmacists and the relative success of each. It would appear, he felt, that the pharmacist has a decided advantage in every way.

This entertaining and instructive talk was closed with a reference to the high desirability of a good library of journals and reference texts in the prescription room of every pharmacy.

Prof. C. L. Cox, in his report for the committee on the Science and Practice of Pharmacy, touched upon the completion and occupation of the headquarters building in Washington, the work of the new Prescription Protective Bureau, recent explanations of the alcohol regulations, proposed survey of open prescription departments, and the revised Tugwell Bill. R. W. Rodman added a few comments about the various substitute bills which have just been introduced into the two houses of Congress, pointing out as he did so, *the futility of intelligent abstracting of the bills for purposes of brief discussions* such as we were permitted in committee reports. This was forcibly driven home by the fact that proponents and opponents in congressional committee sessions, spoke for 4 to 5 hours at a time on the bills.

The speaker of the evening, James A. Bauman, of the State Board of Pharmacy, was then introduced by President Little. He discussed the recent State legislation pertaining to the sale of hypnotic drugs, the new prescription laws, and the Board of Pharmacy regulations resulting therefrom.

He brought out the fact that some of the Board regulations relative to the prescription law were forerunners of legislation planned to strengthen the professional standing of the pharmacists of New Jersey.

The formal discussion finished, Mr. Bauman answered many questions of procedure which had been bothering pharmacists since the enactment of the new laws. C. Graham McCloskey, also a member of the State Board, was present and gladly coöperated with Mr. Bauman in handling the flood of questions.

We greatly appreciated the presence of these two men and hope that they will bring their colleagues and meet with us often.

The meeting adjourned after Mr. Rodman had announced that Dr. James C. Munch, of Sharp and Dohme, would be the speaker at our next gathering.

L. W. RISING, *Secretary.*

NORTHERN OHIO.

The regular monthly meeting of the Northern Ohio Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held on February 9, 1934. Featured as a dinner meeting in the dining room of the Western Reserve University Faculty Club, it proved to be a very profitable affair for the score or so of prescription pharmacists who were present, besides the faculty members of Western Reserve School of Pharmacy.

The first half of the business meeting was taken up by a review of the literature dealing with iron medication. Prescription suggestions were approved for use in the makeup type prescriptions to be distributed among the 1400 physicians of the Cleveland Academy of Medicine.

The second half of the meeting was given over to reports by members on their recent efforts in detailing physicians. The various viewpoints and criticisms of both physicians and pharmacists were made to serve a very useful purpose in the formulation of additional methods of approach.

All the members present were highly gratified with the results so far attained. Evidence that the initiative shown by the members in detailing physicians will bring results is indicated by the active coöperation of the Cleveland Academy of Medicine and the recent applications for membership to the Northern Ohio Branch of the A. PH. A.

NEIL T. CHAMBERLIN, *Secretary.*

NORTHWESTERN BRANCH A. PH. A.

In connection with the Golden Anniversary Meeting of Minnesota Pharmaceutical Association there was held a joint session of the Scientific and Practical Section and the Northwestern Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION.

A condensed program of the session follows:

Address of chairman, Dean Frederick J. Wulling. Reports of the following committees: College of Pharmacy, J. L. Fitzgerald, chairman; Drug Plant Culture, G. J. DeMars, chairman; Practical Pharmacy, J. B. Slocumb, chairman; Professional Standards by A. R. F. Johnson; Interprofessional Relationships, H. H. Gregg, Jr., chairman; Research, Dr. Charles H. Rogers, chairman; Hospital Pharmacists, Sister St. George, chairman; U. S. P. and N. F. Revision, F. A. Upsher Smith, chairman; Adulterations, Rugnar Almin, chairman; Public Health, H. O. Tiegen, chairman; Fellowship, C. T. Heller, chairman; Rho Chi, George Crossen; Historical, Dean F. J. Wulling, chairman. Report of Minnesota Pharmaceutical Educational Conference, F. J. Wulling. College of Pharmacy, University of Minnesota, Annual Historical Report, F. J. Wulling. Paper on Professional Pharmacy, Theodore A. Arneson. Iodine Standards, Oscar F. Muesing. Fifty Years of Personal Observation in the Advance of Pharmacy, George Countryman. Report on N. F. Revision Work, Gustav Bachman. The Pharmacist and the NRA, N. Vere Sanders. A Paper, George T. Kermott. The Art of Compounding, David F. Jones. The Significance of Business History, Willoughby Babcock. Another Patent Medicine Era, Joseph Vadheim. Report on M. S. Ph. A. Fellowship, Karl Goldner. A New Deal for American Pharmacy, Anton Hogstad, Jr. Biennial Report, College of Pharmacy, University of Minnesota, F. J. Wulling. Historical Pharmacy in Minnesota, F. J. Wulling. Presentation of M. S. Ph. A. Scholarship Token, President Anderson. The Pharmacognosy of Animal Drugs—A New Field of Pharmacognostical Study, E. B. Fischer. A Paper, Edward Brecht. The Influence of Standardizing Agencies in Education, F. J. Wulling. The M. S. Ph. A. High Spots—Semi-Centennial, F. J. Wulling. Pharmacognostical Investigations of Chrysanthemum Balsamita var. Tanacetoides and Chrysanthemum Balsamita (Balsamita vulgaris), E. B. Fischer. A Brief Paper, John Connell.

A conference of the National Association of Boards of Pharmacy and the American Association of Colleges of Pharmacy was held on the same day, February 15th.

PHILADELPHIA.

The January meeting of the Philadelphia Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held at the Temple University School of Pharmacy, on Tuesday evening, January 9th.

President Eby called the meeting to order and announced the program as a Symposium on the new Hormone—Tissue Extract.

Dr. James C. Munch, Associate Professor of Pharmacology at the School of Pharmacy, Temple University, was introduced, and began a discussion of the preparation and pharmacology of Tissue Extract. The following information was brought out in Dr. Munch's talk.

Tissue Extract is found in the pancreas, liver and kidneys, and is excreted in the urine. Before the discovery of this hormone, insulin was sometimes used in the treatment of hypertension, but it was found that in extraction of the pancreas an impure insulin was obtained containing some Tissue Extract, and that this, and not the insulin was responsible for the fall in blood-pressure.

The active principle of Tissue Extract is a vasodilator, and a direct antagonist to epinephrine. Its unit value is determined by its

epinephrine-neutralizing effect. When epinephrine is injected it produces a constriction of the arteries and a rise in blood-pressure. Tissue Extract counteracts this effect. One cc. of Tissue Extract is standardized to counteract the effect of 0.01 mg. of epinephrine.

Dr. Munch's assistants prepared an anæsthetized dog, its blood-pressure being recorded on a kymograph. Epinephrine was injected and the rise in blood-pressure noted. Then injections of Tissue Extract were made and the counter-effect was apparent on the recording device.

President Eby then introduced Dr. Joseph B. Wolffe, Associate Professor of Medicine at the Temple University School of Medicine. Dr. Wolffe's discussion concerned the clinical phases of the Tissue Extract. He spoke of the considerable interest at the present time in various forms of heart disease, especially angina pectoris, or the construction of the coronary artery. High blood-pressure comes on gradually, and the arteries are often hardened and blocked before serious symptoms are apparent. Angina pectoris is caused by indiscretions in dietary habits, excessive use of tobacco, etc. Dr. Wolffe has successfully treated causes of angina pectoris with Tissue Extract, and finds that in 55% of the cases clinical relief was obtained, 30% were partially relieved and 15% were failures. The hormone is injected intramuscularly or subcutaneously in doses of 2 to 5 cc., each cc. representing 10 units.

Special diets are used in conjunction with the Tissue Extract, depending upon the type of patient. Dr. Wolffe's talk was illustrated with a series of lantern slides.

The following resolution was presented and adopted:

RESOLUTION ON THE DEATH OF JOSEPH W. ENGLAND.

WHEREAS it has pleased Almighty God to remove by death our Beloved Co-worker and Fellow-member, Joseph W. England, who died December second, and WHEREAS Mr. England served the profession of Pharmacy in many positions of responsibility in both state and national associations, over a period of fifty years, and in his death Pharmacy has lost one who had contributed in many ways to the furtherance of its highest ideals. He was a man esteemed professionally by all who knew him. He graduated from the Philadelphia College of Pharmacy and Science in 1883. In 1886, he was appointed Chief Pharmacist in the Philadelphia General Hospital and in 1900, he became head of the Pharmaceutical Department of the H. K. Mulford Company. He left that position in 1902 to become Scientific Director of Smith, Kline and French Laboratories, Philadelphia. He was widely known for his researches in Pharmacy, and was the author of hundreds of original articles of scientific character and many of an historical nature. At one time he was a member of the Revision Committee of both the U. S. P. and the N. F. He served as curator of the Museum of the Philadelphia College of Pharmacy and Science from 1887 to 1920 and had been a trustee of the institution since 1892, and the chairman of the Board since 1924. In 1903 his *Alma Mater* conferred upon him the degree of Master in Pharmacy, *honoris causa*. From 1893 until his death, he had served as a member of the Publication Committee of the Philadelphia College of Pharmacy and Science and since 1904 had been recording secretary of its Alumni Association. He served as its president in 1891–1892. Other services included the Acting Editorship of the AMERICAN PHARMACEUTICAL ASSOCIATION *Bulletin* in 1910 and 1911, and the chairmanship of the same Association's Committee on Publications. He also had been secretary of the Council of the AMERICAN PHARMACEUTICAL ASSOCIATION. He was the Editor of "The First Century of the Philadelphia College of Pharmacy," a volume widely acclaimed for its accurate and fascinating portrayal of the first one hundred years of this college. In 1926, he was president of the Pennsylvania Pharmaceutical Association, and in 1921–1922 held the presidency of the Philadelphia Branch, A. PH. A.

Resolved, that we express our deep sorrow at his death and extend to his widow and daughter our sincere sympathy in their hour of bereavement.

Resolved, that a copy of this resolution be sent to the family, be spread upon our minutes and be sent to the Editor of the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

E. H. MACLAUGHLIN, *Secretary*.

PITTSBURGH.

The Pittsburgh Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION held a well attended meeting Tuesday evening, January 16, 1934, in the main lecture room of the Falk

Clinic. The group had the pleasure of hearing John Russell, X-ray technician of the Falk Clinic; Dr. W. Harry Archer, lecturer in Anesthesia and Exodontia of the School of Dentistry, University of Pittsburgh, and Dr. Paul Walker, associate professor of Exodontia and Anesthesia, School of Dentistry, University of Pittsburgh.

Clarence T. Van Meter presided.

John Russell, X-ray technician of the Falk Clinic, presented a very interesting and practical demonstration of X-ray and Fluoroscopic Technique. He showed an instructive film on the manufacture of X-ray plates. In summarizing his presentation, Mr. Russell indicated to the group how very important to health is the necessary coöperation between patient and physician when an X-ray or fluoroscopic examination is needed. The pharmacist can serve in breaking down the idea that there is something mystic or fantastic about X-ray and fluoroscopic diagnosis. The patient must be brought to the realization that it is a very necessary part of complete medical service when it is ordered by the practitioner.

President Van Meter introduced Dr. W. Harry Archer, member of the teaching staff of the School of Dentistry, University of Pittsburgh. Dr. Archer presented a paper entitled "A Discussion of Dentifrices and Mouth Antiseptics." The speaker elected to present the good and bad qualities of certain proprietary articles sold as dentifrices and mouth antiseptics. He stated that, "many dentifrices on the market to-day are unnecessarily and irrationally complex in composition. The sole function of a dentifrice is to aid in keeping the teeth clean by the removal of food débris by the mechanical use of the tooth brush." He cited instances where "the claim for therapeutic or bacteriostatic virtue of some of the dentifrices on the market to-day borders on the ridiculous." He then indicated the formulated provisions of the council of therapeutics of the American Dental Association for the inclusion of dentifrices in "Accepted Dental Remedies." Mention was made that, "The labors of the council of therapeutics are at present directed toward a control of irresponsible claims made in dentifrice advertising, together with the exposure of misbranded and injurious dental nostrums." Dr. Archer said, "I was pleased to note that the code of ethics of the AMERICAN PHARMACEUTICAL ASSOCIATION deals with the subject of nostrums as follows: 'The pharmacist should uphold the approved legal standards of the United States Pharmacopœia and National Formulary and should, as far as possible encourage the use of these drugs and preparations and discourage the use of objectionable nostrums. He should not accept agencies for objectionable nostrums, nor allow his name to be used in connection with advertisements or correspondence furthering their sale.' A number of agents used to whiten teeth are sold directly to the public at drug stores and department stores. In order to make this discussion interesting to you, I made a survey of twenty-five drug stores throughout Metropolitan Pittsburgh, to ascertain what dentifrices were stocked. The results were tabulated and I found that, in spite of all publicity given the harmful products, six out of every twenty-five, or approximately 25%, stocked one or two of the worst dental nostrums on the market to-day. I was gratified to learn that the majority when asked what they had for pyorrhea, advised the individual to have the condition treated by a dentist."

The speaker considered the fact that one drug store stocked 28 different kinds of tooth pastes and powders and 13 mouth washes. "Now it isn't my purpose to tell you how to conduct your business," said Dr. Archer, "but it seemed to me that this pharmacist had a lot of money tied up in seldom called for articles. Now where can he start to eliminate and what can he tell his customers when they ask for certain preparations? Obviously he could not use the classical excuse, 'We do not have that but we do have something better.' I suggest for instance that he could tell a customer who called for a nostrum that he did not stock this product as it has been proved to be injurious to the tooth enamel by authorities and that this code of ethics prohibited him from stocking injurious products." Two benefits would be derived from such a procedure whereby the most glaring nostrums are eliminated from his stock:

"*First:* His stock of non-essential preparations would be greatly reduced allowing him a larger stock of essential preparations.

"*Second:* He would be putting into effect the principles of his code of ethics." At this point the speaker presented the results and findings of investigators of the American Dental Association, and cited instances of over medication with such medicaments as Sodium perborate and alkalies.

"It is disgusting to read in a magazine, or

hear on the radio, the wild, exorbitant claims made for some dentifrice, knowing that they are not the result of conscientious, careful research, but the abortive product of some high pressure advertising manager, whose knowledge of dentistry is obtained from a text book on dental diseases.

"The leading Dental Schools to-day give their students a course in Dental Medicine and Pharmacology. At the School of Dentistry, University of Pittsburgh, this course covers fully all remedial agents that properly belong to the field of Dental Medicine, includes prescription writing and discusses briefly the most important general remedies available in dental diseases and emergencies. The course causes the student to familiarize himself with the dental preparations of the National Formulary. During the Junior and Senior years when the clinical work is done in the infirmary these students write prescriptions for their patients which are countersigned by the instructor, and the patient has the prescriptions filled at the school's pharmacy. When the students graduate they are equipped with sufficient knowledge to enable them to coöperate intelligently with members of the pharmaceutical profession."

The next speaker, Dr. W. Paul Walker, associate professor of Exodontia, University of Pittsburgh School of Dentistry, considered the use of "Analgesics, Anodynes and Sedatives in Dentistry."

Quoting from Dr. Walker's paper:

"One of the large commercial houses, manufacturing a brand of procaine hydrochloride, used in local dental anesthesia, quotes from Hippocrates for its advertising slogan: 'The Alleviation of Pain is a Sublime Task.' We are willing and ready to recognize not only the professional idealism but also the economic value of such an intensely worth-while goal as is the prevention of human suffering. Since time, indefinitely ancient, man has made efforts to alleviate or eliminate pain. From the crude aboriginal method of chewing cacao leaves, and allowing the saliva to drip into the open wound, down to the present-day multiplicities of anesthetics, sedatives, anodynes, analgesiques, hypnotics, etc., we follow an ever-broadening field of human endeavor and activity. It has been because of the scientifically correct use of such medicaments at hand, and the constant striving to eliminate the useless and deterrent methods, that the science of materia medica, therapeutics and pharmacology has advanced so greatly along this line.

"Along with the true accomplishments in the discovery and perfection of really valuable drugs and remedies have come also a host of others developed for selfish commercial purposes. So many, indeed, have been the preparations perfected that even the most experienced professional man occasionally is lead astray by these modern medicinal gold bricks. It is with the thought of upholding a higher ethical standard, in that the worthless be eliminated in favor of the truly valuable, that I enter upon this subject."

Dr. Walker then formulated the following classification:

1. *Analgesics* — produces insensibility to pain.
2. *Anodyne*—relieves or assuages pain.
3. *Sedative*—moderates or tranquilizes excitement.

In further consideration of his subject, Dr. Walker indicated how important it is for the prescriber to be thoroughly familiar with the pharmacology, posology and toxicology of the drug.

The therapeutic classification Dr. Walker presented was very complete. The official medicinal and remedial agents possessive of the aforementioned therapeutic properties were particularly emphasized. Those preparations which are acceptable to the American Dental Association and to the Council of Chemistry and Pharmacy of the American Medical Association were stressed. Those to which some objection was raised, were also discussed.

In summation Dr. Walker is quoted, "Simplified and rational therapeutics remains a fundamental law in medicine and in dentistry. These few drugs namely, barbital, phenobarbital, phenacetine, amidopyrine, antipyrine and acetylsalicyclic acid, etc., have not lost their therapeutic value by the formulation and preparation of so-called substitutes. It is, of course, necessary that open mindedness be used in considering new remedies of value, but it is of paramount importance that the old and valuable shall not be discarded for some new and questionable. It is to be hoped and desired that a conscientious effort on the part of the professional man be evidenced in bringing about this valuable reform, in drug usage and manipulation which is so intensely necessary at this time."

The papers were briefly discussed by Dean C. Leonard O'Connell, and an invitation extended to the guest speakers for a joint session of the Pittsburgh Branches of the Dental and Phar-

maceutical Societies. It is hoped that this can be arranged soon.

On motion, a rising vote of thanks was accorded those who participated in the evening's program.

President Van Meter presented to the group Dr. George D. Beal, Assistant Director of the Mellon Institute of Pittsburgh, who has recently been elected to serve as First Vice-President of the AMERICAN PHARMACEUTICAL ASSOCIATION. Dr. Beal acknowledged the introduction.

The officers and members of the Pittsburgh Branch were pleased to have as their guest so many members of the student's branch of the Pittsburgh College of Pharmacy. A cordial welcome is extended to all pharmacists to participate in the activity of the Pittsburgh Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION.

FRANK S. MCGINNIS, *Reporter.*

JOINT PHARMACY MEETING IN BALTIMORE.

The Maryland Pharmaceutical Association and the Baltimore Retail Druggists' Association held a joint meeting at the Hotel Emerson, Baltimore, February 14th. It will long be remembered as a most helpful pharmacy meeting; the attendance was fine and the addresses of unusual brilliance and worth. President L. V. Johnson, of the State association, and President Simon Solomon, of the City association, presided. The afternoon session, was devoted entirely to a discussion of business problems.

Editor Jerry McQuade delivered a stirring address. He covered hurriedly the conditions surrounding the preparation of the retail drug code, expressed the feeling that the code was worthless and characterized it as a "price cutter's code." He gave special attention to some very recent developments which are being worked out by manufacturers, independent retailers and chains, to bring about a better price situation throughout the country. The plan will be under the local supervision of a committee to be selected. Mr. McQuade expressed himself as convinced that the plan would bring about much sounder business conditions.

Nelson A. Miller, of the United States Department of Commerce, spoke on "The Economic Situation in the Drug Business." Mr. Miller has been associated with the St. Louis Drug Store Survey for several months and much of his talk dealt with the facts and figures established by that study. One very interesting thing brought out by him was his feeling that business conditions strongly indicate that retail pharmacists may anticipate a pick up in business of 30 to 35 per cent.

Prof. Marvin Andrews, University of Maryland, gave an up-to-date picture of the work being done by the Committee on U. S. P. and N. F. Publicity of which he is chairman, and submitted samples showing the many combinations suitable for prescribing official drugs, he also referred to methods of dispensing proprietaries.

President Aquilla Jackson, of the Local Retail Drug Trade Council, presented a report which was well received, which evidenced the confidence of the pharmacists in the members of the Council.

The evening meeting was given over to a discussion of professional matters. Two valuable addresses were delivered. Dr. G. O. Sharrett, Cumberland, president of the Medical and Chirurgical Faculty of Maryland, delivered a most impressive talk. It was an earnest, candid and fearless talk and went to the very heart of many important problems.

Chairman E. Fullerton Cook, of the Committee on Revision of the United States Pharmacopœia, discussed the professional phases of pharmacy and gave special attention to the procedure followed in revision work.

President Frank L. Black, of the Alumni Association, School of Pharmacy, University of Maryland, presided over the evening session.

Michael Joseph Dausch, of Baltimore, has been awarded an annual membership in the AMERICAN PHARMACEUTICAL ASSOCIATION, following a precedent of former years.

ASSOCIATION BUSINESS

AD INTERIM BUSINESS OF THE COUNCIL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 1934–1935.

Office of the Secretary, 2215 Constitution Ave., Washington, D. C.

LETTER NO. 6.

February 2, 1934.

To the Members of the Council:

34. Contract for Printing and Mailing the Journal of the A. Ph. A. for 1934. Motion No. 7 (Council Letter No. 5, page 65) has been carried and the contract has been awarded to the Mack Printing Company.

35. Budget for 1934. Motion No. 8 (Council Letter No. 5, page 66) has been carried and the budget approved as submitted.

36. Selection of Auditors. Motion No. 9 (Council Letter No. 5, page 67) has been carried and the accounts for 1933 are now being audited by W. A. Johnson & Co.

37. Election of Members. Motion No. 10 (Council Letter No. 5, page 67) has been carried and applicants numbered 57 to 74, inclusive, are declared elected.

38. The Headquarters Building. The removal of the offices and records of the ASSOCIATION from 10 W. Chase St., Baltimore, Md., to the Headquarters Building, 2215 Constitution Ave., Washington, D. C., was completed on January third. The approach steps have been completed and the work on the grounds is progressing very satisfactorily. The widening of Constitution Avenue is completed and the sidewalks will be laid within a short time unless the weather prevents.

39. Use of the Text of N. F. V. The following letter has been received from Chairman DuMez of the Committee on Publications:

> "For the past two decades, to my knowledge, Gould's Medical Dictionaries have been granted permission to use portions of the text of the National Formulary in the different editions of the dictionaries published by them, so I can see no reason why it is necessary for the Committee on Publications to again vote on this matter. I will, therefore, recommend that permission to use portions of the text of the National Formulary in the publication of the different editions of Gould's Medical Dictionaries be granted with the understanding that notice of the permission received be printed on the rear of the title page of the books published, and that the ASSOCIATION charge the customary fee of $5 for this privilege."

(*Motion No. 11*) *It is moved by DuMez that the P. Blakiston's Son & Co., Inc., be given permission to use portions of the text of the National Formulary V in the preparation of Gould's Medical Dictionaries, and at the usual charge of $5.*

40. American Association for the Advancement of Science. The fall meeting for 1933 was held in Boston, Mass., Dec. 26–29, 1933. Dr. John C. Krantz, Jr., was appointed Councilor to this association for 1933–1934 by President Swain and attended the meeting as the representative of the AMERICAN PHARMACEUTICAL ASSOCIATION which is affiliated with Section N, Medical Sciences.

The AMERICAN PHARMACEUTICAL ASSOCIATION, by invitation of the officers of Section N, held a joint session with the American College of Dentists on Friday morning, as one session of Section N. The program follows:

> Friday Morning, Joint Session with the AMERICAN PHARMACEUTICAL ASSOCIATION and the American College of Dentists, December 29, 1933, 9:00; John Ware Hall, Boston Medical Library, 8 The Fenway.
>
> John C. Krantz, Jr., Second Vice-President, AMERICAN PHARMACEUTICAL ASSOCIATION, Presiding

1. "Pharmacy and Dentistry in Therapeutic Progress." Harold S. Smith, chairman, and Samuel M. Gordon, secretary, Council on Dental Therapeutics, American Dental Association.

2. "An Investigation of the Viburnums and Their Medical Aspects." Heber W. Youngken, Massachusetts College of Pharmacy.

3. "Certain Scientific Aspects of Pharmacopœia Making." E. Fullerton Cook, chairman of the Committee of Revision of the United States Pharmacopœia.

4. "The Determination of Magnesium by Alkalimetric Titration." Milan A. Logan, Forsyth Dental Infirmary for Children and Harvard Medical School.

Dr. Krantz reports that the joint session was well attended and that the papers and their discussion were very interesting. This is the first time that the AMERICAN PHARMACEUTICAL ASSOCIATION has participated in a program and the fine coöperation of Drs. Krantz, Youngken and Cook is acknowledged. No doubt but that this step will lead to a closer contact with the A. A. A. S. and its interest in the work of the AMERICAN PHARMACEUTICAL ASSOCIATION and in the scientific work being done in pharmacy is very encouraging.

41. American Joint Committee on Horticultural Nomenclature. Dr. Heber W. Youngken submits the following report:

"I attended the meeting of the American Joint Committee on Horticultural Nomenclature held for the purpose of planning the revision of *Standardized Plant Names* at the Hotel New Yorker, New York City, on January 15th, and took an active part in the two sessions of this organization.

"I shall prepare a detailed report of the proceedings of this meeting as a part of my annual report of the Committee on Horticultural Nomenclature to be submitted to the House of Delegates of our ASSOCIATION at its coming meeting in Washington. However, for the present information of the President, the Council and yourself, I am pleased to state it was voted to revise and enlarge the scope of *Standardized Plant Names* so as to include the scientific and common name of every plant yielding a drug, spice or dye in American commerce as well as some other economic products, and your committeemen present were requested to submit a complete list of the common names of medicinal plants which the AMERICAN PHARMACEUTICAL ASSOCIATION desires included in the revision of this work. The delegates present representing all but one of the constituent organizations showed marked interest in the problems of American Pharmacy as related to the work of standardizing plant names especially synonyms, and officers and members alike appeared desirous of granting our requests for changes and additions to the present work, which will extend its usefulness to the entire drug trade.

"I feel convinced that if all the plans for the revision of that work are carried out which were adopted at the meeting of January 16th, the edition will prove a classic work on standardized plant names, and its adoption as such by a greatly increased clientele is anticipated. The present work has already become the standard for plant names covered in a number of organizations and in the Dept. of Agriculture."

Dr. Youngken was authorized to attend this meeting by President Swain with the approval of Chairman Hilton of the Council.

42. Buckram Binding for N. F. VI. In order to secure the cloth required for the binding of Series A, 25,000 copies of the N. F. VI before the advance in price, the Mack Printing Co. purchased the cloth in July 1933, and will store it without charge until used. They also printed and bound and have carried in stock about 2000 copies of the N. F. V for more than a year, to prevent an advance in price. They now request that the ASSOCIATION give a three months note for the total amount $2587.43—$1026 for cloth and $1561.43 for N. F. V—to be reduced each three months as convenient. The U. S. P. made a similar arrangement for the cloth required.

This suggested arrangement has the approval of Chairman Hilton of the Council.

(Motion No. 12) It is moved by Chairman Swain of the Committee on Finance, that the secretary and treasurer be authorized to execute a note, payable in three months, to the Mack Printing

Company, Easton, Pa., for $2587.43, with interest, and to renew the note, with reductions, as may be necessary.

43. Applicants for Membership. The following applications properly endorsed and accompanied by the first year's dues have been received:

No. 75, W. H. Treiber, Enter Square, Emmitsburg, Md.; No. 76, L. B. Lathroum, 735 E. 20th St., Baltimore, Md.; No. 77, A. A. M. Dewing, Centerville, Md.; No. 78, Charles William Abbott, North Pacific College of Oregon, Portland, Ore.; No. 79, Samuel Harold Culter, 1 Park Ave., Tuckahoe, N. Y.; No. 80, Sister Agnes FitzSimmons, 16th St. & Girard Ave., Phila., Pa.; No. 81, Edith A. Kramer, 2308 N. Fulton Ave., Baltimore, Md.; No. 82, W. Wallace Smith, 125 N. Howard St., Baltimore, Md.; No. 83, Ralph C. Dudrow, Hyattsville, Md.; No. 84, H. O. Wicks, 7401 Harford Road, Baltimore, Md.; No. 85, Frank C. Purdum, 5500 Harford Rd., Baltimore, Md.; No. 86, S. F. Pettis, Canton, Mississippi; No. 87, A. Lester Batie, Laurel, Md.; No. 88, W. H. Clark, Market St., Pocomoke City, Md.; No. 89, H. O. Trowbridge, Kensington, Md.; No. 90, Robert A. Pilson, Main St., New Windsor, Md.; No. 91, W. G. Bridges, 1726 Hountted Rd., Columbus, Georgia; No. 92, Howard B. Lewis, 218 W. Medical Bldg., U. of Mich., Ann Arbor, Mich.; No. 93, Albert William Lewing, 310 Erkenbrecher Ave., Cincinnati, Ohio; No. 94, Marion D. Falconer, 223 E. Alberta, Anaheim, Calif.; No. 95, John F. O'Brien, 365 Winton Rd., Rochester, N. Y.; No. 96, Gleb Alexander Popoff, 1453 7th Ave., Apt. No. 2, San Fransciso, Calif.; No. 97, Henry E. Kleinsorge, Jr., 1439 5th Ave., San Francisco, Calif.; No. 98, Jerome Royal Fletcher, 860 Ashbury St., San Francisco, Calif.; No. 99, Weslie Wilson Brown, 398 Hayes St., San Francisco, Calif.; No. 100, Hoffmann Henry Siebe, 133-A Carl, San Francisco, Calif.; No. 101, Paul Lantrip, 1704 Alabama Ave., Jasper, Alabama; No. 102, Chester Mearl Hauck, 9389 Courvile St., Detroit, Mich.; No. 103, Ernest Berger, First Nat'l Bank Bldg., Tampa, Florida; No. 104, Samuel Schwartz, 600 E. 169th St., New York, N. Y.; No. 105, Ina Lorene Griffith, Faculty Exchange, Norman, Okla.; No. 106, Minoru Masuda, 506½ Maynard Ave., Seattle, Wash.; No. 107, Faheem Minhail, American Mission Hospital, Assiut, Egypt; No. 108, Lawrence Davis, 10,354 12th St. Detroit, Mich.; No. 109, Manasset Kaprielian, Rue Vahr, Beirut, Syria; No. 110, Sister Mary Adelaide, 1026 Belmont Ave., Youngstown, Ohio; No. 111, Everette A. McArthur, % Parke, Davis & Co., Detroit, Mich.; No. 112, William J. Ohland, 17 Durrell St., Verona, N. J.; No. 113, Charles Albert Hudson, 148 S. Court St., Luray, Va.; No. 114, Meyer Harry Goldberg, 1246 Broadway, Lorain, Ohio; No. 115, Norman Carl Fretthold, 1547 Rosewood Ave., Lake Wood, Ohio; No. 116, Joseph Huber, 541 E. 124th St., Cleveland, Ohio; No. 117, Roger K. Lager, 2298 Murray Hill Rd., Cleveland, Ohio; No. 118, Walter Anthony Knurek, 1603 Copassett Ave., Lakewood, Ohio; No. 119, Nicholas Avellone, 2362 E. 79th St., Cleveland, Ohio; No. 120, George B. Merriam, White Sulphur Springs, W. Va.; No. 121, Carl C. Caplan, 1800 Penna. Ave., Baltimore, Md.; No. 122, B. M. Brown, Lyons, Georgia; No. 123, R. M. Birely, St. Paul & 33rd Sts., Baltimore, Md.; No. 124, Godfrey D. Kroopnick, 930 Whitelock St., Baltimore, Md.; No. 125, Irving Freed, 930 Whitelock St., Baltimore, Md.; No. 126, Howard Hollingsworth, College Sta., Box 37, Pullman, Wash.; No. 127, John Russell Vibber, College Sta., Box 668, Pullman, Wash.; No. 128, William Tombari, College Sta., Box 356, Pullman, Wash.; No. 129, Maison Gabriel de Navarre, 12,206 Mendota Ave., Detroit, Mich.; No. 130, Elvira Marjorie Silveira, 3820 Shafter Ave., Oakland, Calif.; No. 131, John H. Beeler, Vinton, Louisiana.

(*Motion No. 13*) *Vote on Applications for membership in the American Pharmaceutical Association.*

E. F. KELLY, *Secretary.*

LETTER NO. 7.

February 2, 1934.

To the Members of the Council:

44. Time of the 1934 Meeting. Since the Madison meeting, careful consideration has been given to the best time for the Washington meeting and for the dedication of the Headquarters Building.

The Government has been engaged in a number of improvements in the area surrounding our site which, unless completed, would have interfered with the dedicatory exercises. These are either completed or are so far advanced as to be finished by April first.

Due to the open weather, the grading and topsoiling of our grounds are practically completed and a good part of the planting. The remainder of this work will be completed by April first, probably earlier. It is, therefore, now assured that these matters will not interfere.

The District of Columbia Pharmaceutical Association has taken great interest in the arrangements for the meeting and is giving splendid coöperation through its officers and members. The local organization is prepared to arrange for the meeting either in the spring or later.

Chairman Dunning has favored holding the meeting in the spring, as expressed in the letter from him quoted below, but his recommendation could not be laid before the Council until the matters referred to above were satisfactorily adjusted. Dr. Dunning's letter is as follows:

> "I consider it of the utmost importance that the dedication of the American Pharmaceutical Headquarters Building takes place in the spring of the year, preferably during the month of May, and that the American Pharmaceutical Association Convention should take place at the same time. The building was occupied and began to operate in January. You will realize that when the building is opened to the public and to our membership and those especially interested in the work of our ASSOCIATION, it will be difficult to maintain enthusiastic interest over a considerable period of time. Many of those whom we wish to interest in making subscriptions to the necessary maintenance fund, especially those whom we hope will make substantial donations, will have seen the building, accepted it and will have, by fall, lost the first flush of their interest. It seems obvious that the occupancy of the building should be quickly followed by its dedication and, thereby, avoiding any possible loss of enthusiasm or interest among those whom we are hopeful will provide the necessary funds to assure financial security.
>
> "There should be no more difficulty in arranging for the meeting of the ASSOCIATION in the spring of 1934 than has been occasioned in having the meeting take place simultaneously with the Pharmacopœial Convention at the same time of the year.
>
> "I hope that the Council will approve my recommendation. I would consider it most unfortunate if they did not."

Dr. Dunning also requests that emphasis be placed on the fact that more satisfactory arrangements for the dedication can be made in the spring when many of those whom we wish to have present, *including Government officials*, will be in Washington.

In the mean time, the views of the A. A. C. P. and of the N. A. B. P. were requested. Chairman Jordan consulted the Executive Committee of the A. A. C. P. The concensus of opinion was in favor of the usual time for the meeting, late in August or early in September, and that a meeting in May will seriously interfere with the attendance from the colleges and also with the program of the A. A. C. P. The following is the closing paragraph of the last letter received from Chairman Jordan:

> "I think I have sent you enough of these comments to let you know that the school men are very much opposed to an early meeting, and I think you can see why this is true. I sincerely hope and trust that arrangements can be made that will be satisfactory to you and that will not call for a meeting prior to June 15th."

A meeting late in June would bring serious conflict with the annual meetings of a number of state associations which occur late in that month.

President Gilbert and Secretary Christensen, of the N. A. B. P., express the belief that a May meeting will lessen the attendance from the boards and will interfere with their program.

The general expression of opinion as secured from a number of individuals consulted, is that a meeting in May would be favored largely because of the dedication of the building and that the latter consideration should be paramount in reaching a decision for this year. A number also favor a meeting in May in Washington because of weather conditions and because the City is more beautiful at that time than later.

Satisfactory hotel and other arrangements can be made for the week of May 7th–12th which will be the most satisfactory time for the meeting if May is selected, as these dates will conflict

least with the colleges of pharmacy and the boards, and corresponds to the time at which the U. S. P. Convention is held.

(*Motion No. 14*) *It is moved by Dunning that the Eighty-Second annual meeting of the A. Ph. A. and affiliated organizations be held during the week of May 7 to 12, 1934.*

In view of the necessity for an early decision, the chairman of the Council has approved the calling of a vote at this time. If there is objection or if any member of the Council desires to comment the vote will be considered as tentative.

E. F. KELLY, *Secretary.*

REPORT OF THE CHAIRMAN OF THE COMMITTEE ON PATENTS AND TRADE-MARKS.*

BY F. E. STEWART, CHAIRMAN.

The time has come for me to resign as chairman of the Committee on Patents and Trade-marks after many years of service in that capacity. However, before doing so, I may be of service in calling attention to some of the important points that have been developed in relation to these laws as applied to pharmacy. Attention has been repeatedly called to the fact that the object of the patent laws as defined in the Constitution of the United States is "to promote progress in science and useful arts." I do not believe that any person who is informed on the subject will contend that the patent laws of the United States as now applied to pharmacy have promoted progress in the science of the materia medica and related and mutually dependent arts of pharmacy and pharmaco-therapy. The law requires that to be patentable an alleged invention must be an invention in fact and that the application for patent grant must "contain a written description of the invention, and of the manner of making, constructing, compounding and using it, in such full, clear, concise and exact terms as to enable any person skilled in the art or science to construct and use the same." It is perfectly evident that materia medica patents are granted by the Commissioners of Patents without complying with this requirement. The patent law also requires that "Every patent shall contain a short title or description of the invention or discovery, correctly indicating its nature and design." Is this requirement complied with? And there are other important requirements. Are they complied with? Send to the Patent Office for a copy of any patent relating to the materia medica and find out. Copies can be obtained at the cost of a few cents. And, if you find that these and other requirements demanded by the patent law have not been complied with, remember that the patent is void and can be revoked. You will find, by referring to the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, Vol. 20, No. 1, January 1931, the report of our committee in which these and other requirements for obtaining patents are stated. For the sake of all concerned, pharmacy therapeutics, pharmaco-therapeutic literature, the U. S. Pharmacopœia, the educational institutions related to pharmacy and medicine, the practitioners of medicine and pharmacy and the public health, why not investigate the methods of the Patent Office in regard to the patenting of materia medica products and preparations and force the Patent Office to comply with scientific, professional and legal requirements in relation to the granting of patents for medical and pharmaceutical inventions.

And the same relates, also, to the registering of trade-marks. Refer for information on the requirements of the trade-mark law to the same report of our committee. Find out what these requirements are and force the Patent Office to comply with them. There is no use for you to consult your lawyers about it. Consult "Browne on Trade-marks" and find out for yourselves what is required. Consult first the report of this committee and then read up in Browne's excellent work on the subject. After you have posted yourselves in this matter then appoint a disinterested committee of pharmacists and physicians and reputable manufacturing pharmacists for further study and consideration of the subject and then decide how best to force the powers that be to play square with all concerned.

A vote of appreciation for his long and useful services was given Dr. Stewart.

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* Madison meeting, A. PH. A., 1933.

EIGHTY-SECOND ANNUAL MEETING, AMERICAN PHARMACEUTICAL ASSOCIATION AND AFFILIATED ORGANIZATIONS AND DEDICATION OF THE AMERICAN INSTITUTE OF PHARMACY, WASHINGTON, D. C.—MAY 7–12, 1934.

The Council of the AMERICAN PHARMACEUTICAL ASSOCIATION has approved May 7th–12th as the dates for this important meeting because it is desirable to have the dedication exercises as promptly as possible, and at this time, which corresponds to that of the U. S. P. Convention, it is probable that many of those whom it is desired to have present, including Government officials, will be in Washington. The city is at its best at this period and very satisfactory hotel and traveling rates are being granted.

The Government will have completed very extensive improvements in the area surrounding the Institute, including the widening of Constitution Avenue to eighty feet, and the intersecting streets are being repaved. The grading and planting of the grounds will be completed early in the spring and the Building is now being furnished and equipped.

Everything will be in readiness for this very noteworthy occasion for American Pharmacy when its permanent home and headquarters will be dedicated and when important plans will be considered for the work to be carried on in the Institute.

The members of the District of Columbia Pharmaceutical Association will act as hosts to the visiting pharmacists and their families and friends. The general committee of arrangements, headed by President Paul Pearson of the District Association, is completing arrangements for the business and entertainment features of the program. The Local Secretary, the Headquarters Hotel and the hotel and transportation rates will be announced at an early date.

In addition to the Meeting and the Dedicatory Exercises, Washington is unusually interesting and enjoyable to visitors at this time. Congress will probably be in session, all public buildings will be open, and the splendid improvements made in recent years in your Capital City will be well worth seeing. The improvements completed and in operation in the Lincoln Memorial section emphasize what a wonderful site the American Institute of Pharmacy occupies. It should make every American pharmacist prouder of his calling because Pharmacy has such a commanding position for its headquarters and a building in full keeping with the splendid surroundings.

FOOD, DRUG AND COSMETIC LEGISLATION.

Nothing definite can be said regarding the outcome of food, drug and cosmetic legislation now in Congress. Senator Copeland modified the bill introduced by him, it was referred to a sub-committee and considered later by the Senate Commerce committee. As a result, it is reported that Senator Copeland will revise his bill and a hearing will be held February 27th, 10:00 A.M., briefs may be filed prior to that hour. The announced plan is to limit the witnesses to five, one to speak on general food and drug legislation and one representing each of the four groups: Foods, drugs, cosmetics and advertisers. Each group will assemble material and designate a speaker to present its argument.

Senator Stephens and Congressman Black are sponsors for the Drug Trade Conference bill; Representative Virginia E. Jenckes, of Indiana, has introduced the bill prepared by Charles Wesley Dunn.

The hearing on February 27th will bring about a discussion of important points as viewed by the administration and of those not fully in agreement therewith. It is to be hoped that the hearing will develop an acceptable measure or supply information which will enable Congress to amend the present law or enact a new measure. It is not helpful to comment further at this time nor of great value to discuss features of the proposals. The proposed bills have brought out constructive thoughts but in some respects have complicated the proposed legislation, the importance of which deserves rational accord and not needless discord.

Several speakers discussed the legislation before New York Branch AMERICAN PHARMACEUTICAL ASSOCIATION, abstracts of these discussions appear in this issue of the JOURNAL.

BALTIMORE BRANCH, A. PH. A.

The February meeting of the Baltimore Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION will be held at the Hotel Emerson on Tuesday, February 27th.

John A. Strevig, of the Eli Lilly and Company, Indianapolis, will present a sound film on: "The Production and Clinical Application of Insulin."

PRIZE-WINNING PHARMACY WEEK WINDOW, 1933.

The background of the window will be recognized as the "famous misnamed picture" described in the March JOURNAL for 1931, pages 236–246, entitled, "The Laboratory," from an

The Prize-Winning Window, Pharmacy Week, 1933.

engraving by J. D. Murray, of a painting by William Hunt. At the left the sources of drugs are shown by connecting specimens with the globe. In the picture are utensils used in prescription work and a dosage illustration is made by showing a bottle of Solution of Magnesium Citrate and a 1/400th grain of aconitine.

O. U. SISSON.

Different forms of administration are shown and the foreground refers to a prescription from the Bible of the year 1491 B.C., which gives the ingredients for an anointing oil.

Mr. Sisson's certificate and other personal records are displayed in the window.

After completing the high school course in Schuyler, Nebraska, Mr. Sisson entered the Chicago College of Pharmacy and graduated in 1894. In 1898, he opened a pharmacy at 5034 Cottage Grove Ave., Chicago, later, he established a pharmacy on the second floor of 841 E. 63rd St.

Mr. Sisson holds membership in national, state and local associations and takes an active part in U. S. P. and N. F. revision. He keeps in touch with the Chicago Medical Society and during the time of the Pharmacy Exhibit at "The Century of Progress" he gave his services for a day or more of each week.

He adheres to ethical advertising that embodies accurate and truthful statements. He believes in giving credit to his employees for the work they do; thus, in a letter he refers to the part which two of his assistants had in making the window display, namely, Rollin Reineck and L. B. Jobusch.

Mr. and Mrs. Sisson have two sons and a daughter. The former are attending the Armour Institute and the daughter is a student at the University of Chicago.

EDITORIAL NOTES

OPPORTUNITIES FOR PHARMACEUTICAL ORGANIZATIONS TO SHARE IN THE HEADQUARTERS.

Chairman H. A. B. Dunning in his address at the Madison meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION, referring to the progress of the American Institute of Pharmacy, said:

"Three State associations have contributed special funds for designated purposes. The Texas Pharmaceutical Association for furnishing the offices of the Editor, the Maryland Pharmaceutical Association for furnishing the offices of the Secretary, and the Kansas Pharmaceutical Association have not as yet decided for what their fund is to be used. Suitable acknowledgment will be made of these splendid contributions and it is hoped that the other state associations will make contributions for special purposes, thus emphasizing the close relations between them and the AMERICAN PHARMACEUTICAL ASSOCIATION and associating the name of each of them with the project."

The dedication of the Headquarters and the annual meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION in Washington will bring ideas forward for sharing in the great work for American pharmacy. It is hoped also to have complete sets of state and national proceedings, laws applying to pharmacy, histories of early pharmacy, photographs of pharmacists who had a part in the development of pharmacy. Individuals have copies of rare and old books which may serve a larger purpose if made part of the library or museum.

CODE AUTHORITIES' CONFERENCE.

A Code Authorities' Conference will convene in Washington, March 5th–8th. President Roosevelt will address the first session, followed by Administrator Johnson. The opening meeting will be held in Constitution Hall, among the considerations are named the possibilities of increasing employment, protections against destructive competition and excessive prices and monopolistic tendencies; the elimination of inequalities and inconsistencies in codes, the position of small enterprises and the many problems of code administration.

In his invitation the Administrator asked for information concerning the effects of codes on operations, including employment, in each industry; on general price trends of products in each industry; and on unethical trade practices, as well as the effects of code provisions, if any, restricting production through limitation of machine hours or plant facilities, and the effect of codes on smaller concerns in each of the industries.

In addition, the invitation solicits suggestions to be presented during the conference for the modification, elimination or addition of specific code provisions; proposals for the elimination of overlapping of codes and for the financing of industry code administration.

REPORT OF THE BUREAU OF NARCOTICS.

The report of the Bureau of Narcotics has been issued in booklet form. Editorial comment was made on page 278 of the April JOURNAL, 1933, on "The Narcotic Control Agreement" and, in the July issue, page 596, on "The Ratification of the Narcotics Limitation Congress." President Franklin D. Roosevelt has signed the agreement ratifying the Convention of Geneva on Narcotic Drugs.

The comments referred to speak in a general way of this great work in control of the narcotic evil, to lessen the number of habitués and impress the harmfulness of misuse of narcotics and the report testifies to the possibilities of coöperation in public health matters. Commissioner H. J. Anslinger has been doing effective work and on a number of occasions has spoken in appreciation of the coöperation of pharmacists.

TONICS.

A meeting of the Guild of Public Pharmacists (Great Britain) was held on January 17th, Mr. H. N. Linstead (secretary of the British Pharmaceutical Society) in the chair. There was a large attendance to hear Dr. J. H. Burn give a lecture on "The Pharmacological Action of Some Well-Known Drugs." Professor Burn dealt in a most interesting manner with various drugs used as tonics and diuretics. The word "tonic," he said, "was in common use not only among laymen but also among pharmacists and doctors; it was therefore of interest to consider what was meant by a word which was used in many different senses. Substances so varied as gentian, strychnine, adrenaline, alcohol, thyroid and vitamin B might all be classed as tonics, and even then the list was incomplete. When the heart was removed from the body and made to beat by saline infusions, the application of strychnine had no effect. The beat of the heart in the body was improved by strychnine, but to understand this, one must consider the connection of the heart with the arterial system."

REVISION OF BRITISH PHARMACEUTICAL CODEX.

Under the direction of the council of the Pharmaceutical Society of Great Britain, reports are being issued preliminary to revising sections of the "British Pharmaceutical Codex." The report of the pharmacy subcommittee presents a summary of the principal new or revised formulas recommended by it for inclusion in the revision. The sub-committee recommends the inclusion of formulas for a number of preparations from earlier pharmacopœias which are not included in the British Pharmacopœia of 1932, but are still in more or less frequent demand.

THE NEW SWISS PHARMACOPŒIA.

The new Swiss Pharmacopœia omitted 108 articles from the previous edition and has added 304 new articles, they include chemicals that are now required in medical practice. Very few drugs of animal origin have been officially recognized.

The Swiss government signed the international agreement for the unification of the formulas of potent drugs with reservations permitting the Swiss Pharmacopœial Committee to deviate from the strengths of galenical preparations laid down in the agreement and also permitting variations in the nomenclature required by the agreement. Nineteen articles of the Pharmacopœia differ from the requirements of the international agreement.

The general principles of nomenclature of the previous pharmacopœia are followed. In some instances the British and the United States pharmacopœias have been drawn upon for titles. Standards for seventy drugs of formulas officially recognized are included. Vegetable drugs are carefully described, but only few biological tests have been adopted; for digitalis, the digitoxin chemical test is given.

THE ESSENTIAL OILS OF THE SWISS PHARMACOPŒIA.

Ernest J. Parry in the *Chemist and Druggist* states "there are twenty-seven essential oils described in the fifth edition of the Swiss Pharmacopœia. Their description is preceded by a general monograph headed 'Olea Aetherea,' which purports to give a general account of their more usual adulterants. But treatment of this kind is not suitable for such a work, nor is it of any very practical value in most cases. For example, turpentine is to be detected by the formation of pinene nitrosochloride in the fraction boiling at 155–156°. But all that this really does is to identify the pinene present, which is a natural constituent of many essential oils. Nor are the solubility, specific gravity, boiling point and lævorotation of sufficient value to indicate the use of gurjun balsam, copaiba or cedarwood oils as adulterants. Chloroform and benzene can hardly be said to be adulterants of essential oils, and need not have been mentioned. Refractive indices are not quoted for the oils."

PERSONAL AND NEWS ITEMS.

The *Deutsche Medizinische Wochenschrift* has entered on its 60th year; the occasion is celebrated by a special number which included the *Deutsches Tuberkulose-Blatt*.

The Rotary Club at Austin, Texas, owns the home in which "O. Henry" lived for a number of years. Various patriotic organizations, including the Daughters of the American Revolution, the Daughters of 1812 and the Daughters of the Republic of Texas, have pledged themselves to gather O. Henry relics to be installed in this one of William Sidney Porter's many homes.

It was in Morely Bros. Pharmacy where a counter blotter was found in which O. Henry had written one of his earlier (unpublished) stories.

Prof. Freeman P. Stroup is successor to the late Joseph W. England, as recording secretary of the Alumni Association of the Philadelphia College of Pharmacy and Science.

Dr. Eugene Maier has been appointed chief bacteriologist of the Merck Institute of Therapeutic Research, Rahway, N. J. He was formerly Research Assistant in the Rockefeller Institute and also bacteriologist at Bellevue Hospital, department of pathology.

Dr. A. Richard Bliss, Jr., director of The Research Laboratories of The William A. Webster Company, Pharmaceutical Manufacturers, became vice-president of the Company on February 6, 1934.

Dr. Robert W. Morrison, formerly Associate Professor of Pharmacology in the University of South Carolina, is now assistant to the Director of Research of the William A. Webster Company.

George H. Needham, fellow-member A. PH. A., in San Francisco, has been giving evening courses in microscopy and photomicrography, participated in by pharmaceutical, food and industrial chemists. He is to address the San Francisco Teachers' Association on "Critical Microscopy."

Robert L. Swain, of the AMERICAN PHARMACEUTICAL ASSOCIATION, will deliver the "Founders' Day Address" at the Philadelphia College of Pharmacy and Science, February 23rd. He is to receive the Ph.M. degree, *honoris causa*.

The names of the ten men who stood highest in the vote of 4106 druggists on "What ten men make biggest news in the drug field?" conducted by the *American Druggist*, are: Carl Weeks, H. V. Arny, John W. Dargavel, J. H. Beal, Wheeler Sammons, John H. Goode, Louis K. Liggett, W. Bruce Philip, Charles H. LaWall and E. F. Kelly. Forty-one hundred and six druggists voted.

Samuel C. Henry, former secretary of the N. A. R. D., has been named a member of the Review Advisory Board by National Recovery Administrator Hugh S. Johnson. This Board is to observe the effect of NRA codes upon small enterprises. The Board will meet for the first time February 26th.

Walter G. Hodge has been appointed national director of distribution for the William S. Merrell Company, Cincinnati.

Attention is directed to page 17 of an opening for a pharmaceutical chemist.

TEMPLE UNIVERSITY GOLDEN ANNIVERSARY.

Temple University, of Philadelphia, celebrated its fiftieth anniversary during the week of February 11th. The University has a wonderful history. As is well known, Russell H. Conwell was its founder and the spirit which moved him in this undertaking has resulted in an institution of which Philadelphia may well be proud. A memorial address was delivered on Sunday (February 11th), by Rev. Dr. N. Joseph Toomey in the auditorium of the Temple. Following this a presentation of the Conwell bust, by Boris Blai, was made in the great court of Mitten Memorial Hall.

During the week displays of medical, dental and pharmaceutical products were open to the public; galenicals and processes were exhibited in the laboratories of the School of Pharmacy.

On Wednesday, February 14th, there was a reception by the officers and directors of the pharmacy Alumni Association to the graduates and undergraduates of the School of Pharmacy. At night there was a faculty and alumni banquet to guests and delegates from universities, colleges and associations. The address was delivered by the Hon. R. S. Copeland, U. S. Senator from New York.

A Founders' Day celebration was held on Thursday, when the principal address was made by Dr. Glenn S. Frank, president of the University of Wisconsin.

The late Dr. John R. Minehart, former dean of the School of Pharmacy was for many years an active member of the AMERICAN PHARMACEUTICAL ASSOCIATION.

Dr. H. Evert Kendig is now the dean of the School of Pharmacy.

DRUG-CHEMICAL DINNER.

Reservations for the ninth annual dinner of the drug and chemical trades, to be held March 8th in the Waldorf-Astoria, New York City, under the direction of the Drug, Chemical and Allied Trades Section of the New York Board of Trade, are now twice those of a year ago, according to Joseph Huisking, chairman of the reception committee and head of the drive intended to make attendance cross the 1000 mark this year. Postmaster-General James A. Farley will be the principal speaker and plans call for broadcasting his speech over a national network beginning at ten o'clock.

OBITUARY.

L. C. BRENNER.

L. C. Brenner, 42nd president of the Texas Pharmaceutical Association, member of the AMERICAN PHARMACEUTICAL ASSOCIATION, died January 22nd, at Memorial Hospital, Houston, Tex.

The deceased was born at Wiesbaden, Germany, February 5, 1863. After graduating from the Real Gymnasium, Wiesbaden, he entered the chemical laboratory of Prof. Dr. R. Fresenius and a year later entered the Polytechnicum at Karlsruhe where he studied pharmaceutical chemistry, graduating in 1884. In 1885 he came to San Antonio to visit his brother. For a time, thereafter, he was employed in New Orleans and New York City; coming back to Texas he opened a pharmacy at Belmont, which he operated successfully for three years and then disposed of it to engage in the drug business with J. C. Bright at Gonzales; subsequently, the firm of Brenner and Bright was consolidated with the firm of Peck & Fly under the name of Gonzales Drug Company of which, in 1912, he became the sole owner.

Mr. Brenner was prominently connected with pharmaceutical organization work for more than a quarter of a century. He took an interest in civic affairs, served as alderman of Gonzales and for 15 years was president of its school board. He was a member of the Masonic bodies in which he held presiding offices. The funeral ceremonies at his home, in Gonzales, were largely attended.

The deceased is survived by his widow, six children and nine grandchildren.

E. B. HEIMSTREET.

E. B. Heimstreet died December 16th, at his home in Lake Mills, Wis., after an illness of several weeks, aged 85 years. He was born at Lansingburg, N. Y., January 3, 1818.

Mr. Heimstreet was largely responsible for the organization of the Wisconsin Pharmaceutical Association, serving as secretary for 32 years, and was a former president and secretary of the Wisconsin Board of Pharmacy. He formerly operated stores in Jamesville and Palmyra and was associated with his son, Charles F., in a drug store in Lake Mills until he retired in 1925. He attended the Madison meeting of the A. PH. A.

Dr. Edward Wight Washburn, chief chemist of the Bureau of Standards, died suddenly at his home in Washington, February 6th, of heart failure. He was a leader in research on the so-called "heavy water," and was the first to produce water containing high concentrations of the hydrogen isotype in considerable quantity, by the electrolytic method. He was author of "Principles of Physical Chemistry," published in 1915 and of many research papers.

SOCIETIES AND COLLEGES.

AMERICAN PHARMACEUTICAL ASSOCIATION meets in Washington during week of May 7th.

SCIENTIFIC SECTION, A. PH. A.

Due to the earlier Convention date this year it will be necessary for those desiring to present papers before the Scientific Section to submit the title and a short abstract to the secretary several months earlier than usual. Please give this matter your prompt attention so that a copy of the completed paper will be in the secretary's hands on or before the opening date of the Convention. The officers of the Section desire your continued coöperation.

F. E. BIBBINS, *Chairman*, Indianapolis.
R. L. ROWE, *Secretary*,
c/o Parke, Davis & Co., Detroit, Mich.

SECTION ON PRACTICAL PHARMACY AND DISPENSING.

FIRST CALL FOR PAPERS.

The First Call for Papers, Addresses, etc., to be presented before this Section is addressed to all those interested in the advancement of Practical Pharmacy. As a fitting part of the ceremonies of dedicating the Headquarters Building of the ASSOCIATION, this year's meeting will be particularly important. Therefore every professional pharmacist is cordially invited to take part in making this an outstanding series of sessions.

All titles and abstracts should be forwarded to the secretary as promptly as possible so as to be listed in the program.

M. J. ANDREWS, *Chairman.*
R. E. TERRY, *Secretary,*
715 S. Wood St., Chicago, Illinois.

CONFERENCE OF PHARMACEUTICAL ASSOCIATION SECRETARIES.

To the Secretaries of State Pharmaceutical Associations:

"Our next Conference will be held at the time of the meeting of the A. PH. A. in Washington, D. C. You will have within the next few days copy of proposed questions for discussion, and it is hoped that each of you may find it possible to attend this Conference and take an active part in the proceedings and render your aid in making it possible for this Conference to accomplish the things of which it may be capable."

ROBERT C. WILSON, *President.*
CARL G. A. HARRING, *Secretary,*
20 Glen Road, Newton Center, Mass.

SECTION ON HISTORICAL PHARMACY.

The Historical Section of the AMERICAN PHARMACEUTICAL ASSOCIATION earnestly seeks the help and coöperation of its friends in preparing the historical program for the approaching annual meetings of the ASSOCIATION to be held in Washington.

This meeting will mark the beginning of a new epoch in American pharmacy. We are making history faster than we realize. Our task is to record it just as accurately and as interestingly as possible.

The present forward trends in pharmacy, of necessity, rest upon the past. Every phase of pharmacy which has transpired, although but yesterday, is history. The story of your store, your apprenticeship, your local or state association would make interesting history. Let us have it.

Few professions afford so many angles of interest, for the writer, as does pharmacy. You are asked to contribute to the Archives of American Pharmacy now housed in the new Headquarters Building in Washington.

LOUIS GERSHENFELD, *Chairman.*
C. O. LEE, *Secretary,*
Purdue University, Lafayette, Ind.

SECTION ON EDUCATION AND LEGISLATION, A. PH. A.

With the annual meeting occurring earlier than usual this year, the preparation of a program should begin at once. To this end the officers of this Section are anxious to secure papers dealing with educational and legislative topics. The success of our meetings depends upon an interesting program and this in turn requires the coöperation of the members. A subsequent notice will contain suggestions as to topics but this does not preclude papers on other subjects within the scope of the Section. The joint session with the Conferences of Law Enforcement Officials and State Association Secretaries will be continued and we hope that reports from all states will be received.

Send your title to the secretary at an early date and make this meeting in the national capitol one befitting the dedication of our headquarters building.

G. C. SCHICKS, *Chairman.*
C. W. BALLARD, *Secretary,*
115 W. 68th Street, New York, N. Y.

STATE PHARMACEUTICAL ASSOCIATION MEETINGS, FEBRUARY TO MAY.

Florida—at Daytona Beach, May 29th–31st.
Illinois—May 15th–17th at LaSalle, Ill.
Iowa—in Sioux City, February 21st–22nd.
Kansas—in Salina, April 10th–12th.
Louisiana—in New Orleans, May 12th–19th.
Minnesota—in Minneapolis, February 13th–16th.
Missouri—in Kansas City, April 24th–26th.
Nebraska—in Omaha, May 7th–9th.
Oklahoma—in Oklahoma City, April 17th–19th.
Texas—in Mineral Wells in May; date not fixed.

William D. Thomas, druggist, of Hoosick Falls, N. Y., has been elected to Congress for the twenty-ninth New York District.

William D. Jones has been appointed acting Postmaster of Jacksonville, Fla.

NEW MEXICO PHARMACEUTICAL ASSOCIATION.

New Mexico Pharmaceutical Association will meet May 23rd–24th, in Santa Fe. The convention city was founded by the Spanish in 1605, but it has a prior history as an ancient Indian village, only St. Augustine can claim rivalry in point of years. It is anticipated that the meeting will be largely attended; the New Mexico Board of Pharmacy will meet May 21st and 22nd, prospective candidates should address G. H. Sasser, secretary of the Board for application blanks.

PROFESSIONAL PHARMACY EXHIBIT AT OKLAHOMA PHARMACEUTICAL ASSOCIATION.

Oklahoma Pharmaceutical Association will hold its annual session in Oklahoma City in April. A comprehensive professional pharmacy exhibit will be an interesting feature, similar to the one featured at the convention of the Wisconsin Pharmaceutical Association in Milwaukee.

BOSTON DRUG SHOW.

The first Drug Show, Health Fair and Beauty Bazaar ever held in New England is scheduled during the first week in April at the Mechanics Building in Boston. A large number of the retail drug leaders of New England are lending their support to the show, and the sponsorship of Governor Joseph B. Ely of Massachusetts has been secured.

HISTORY OF BOSTON DRUGGISTS' ASSOCIATION.

Walter R. Doliver has prepared a short history of Boston Druggists' Association in booklet form. Many names familiar to members of the AMERICAN PHARMACEUTICAL ASSOCIATION are included among those who have been and are active in the ASSOCIATION.

DRUGGISTS' CONGRESS IN CONNECTICUT.

Druggists from all parts of Connecticut attended the first Pharmaceutical Congress and Exposition of the Alumni Association of the Connecticut College of Pharmacy at Hotel Taft in New Haven. Ethical and commercial phases of the relation of the pharmacist to the public were considered and speakers and exhibits emphasized the strides made in the compounding of drugs.

Dr. Milton C. Winternitz, dean of the Yale School of Medicine, stressed the close relationship between pharmacy and medicine in the early days of both professions and urged the coöperation of the pharmacists.

FREE ANALYTICAL SERVICE GIVEN BY PHARMACY SCHOOL.

Druggists throughout the state of Oregon are the beneficiaries of a unique service maintained for them at the State College here under the direction of Prof. Lewis C. Britt of the Oregon State College of Pharmacy. A free analytical laboratory has been in operation right on the campus of the College since 1927, to assist Oregon pharmacists in keeping their drugs up to the highest standard of purity.

The pharmacists claim that this is perhaps as close an example of coöperation between registered pharmacy and a college of pharmacy as the profession can show anywhere. Dr. Britt closely collaborates with Linn E. Jones, secretary of the Oregon Board of Pharmacy, by whom all samples submitted by druggists for analysis must be approved. As the state has no pure drug law, the laboratory offers the only means of determining the purity of drugs not sold in the original unbroken packages. The laboratory was established through the efforts of the Oregon State Board of Pharmacy.

NATIONAL ASSOCIATION OF RETAIL DRUGGISTS.

New Orleans has been selected for the 1934 meeting of the N. A. R. D. Dates September 24th–29th. Thomas S. Smith, of Wilmington, Del., has been appointed member of the Executive Committee, succeeding Ambrose Hunsberger of Philadelphia.

NINTH INTERNATIONAL CONGRESS OF CHEMISTRY.

The ninth International Congress of Pure and Applied Chemistry will meet in Madrid, April 5th to 11th. A program has been arranged for April 3rd to 24th, giving those who attend an opportunity to visit interesting places of Spain.

NEW JERSEY BOARD OF PHARMACY.

Examinations for applicants for the Registered Pharmacist Certificate will be held by the Board of Pharmacy of the state of New Jersey on Thursday, April 19th, at the State House, Trenton, according to an announcement from the Board Office.

All applications for the examination must be filed with the Secretary of the Board, 28 W. State St., Trenton, not later than March 19th.

UTILIZING FARM WASTE.

The Iowa State College has completed a new research laboratory devoted to the study of problems in connection with work on waste material, such as corn cobs, hulls, etc.

CHEMICAL MANUFACTURING CODE.

The basic code for chemical manufacturing, prepared and advanced by the Chemical Alliance, was approved by the President, February 10th.

LEGAL AND LEGISLATIVE.

CODE CONFERENCE.

President Roosevelt will address what probably will be the greatest gathering of leaders of industry and trade in the country's history—the conference of Code Authorities and trade association committees scheduled to be held in Washington, March 5th to March 8th.

In his call for the conference, the opening sessions of which are to be held in Constitution Hall, General Johnson outlined the major purposes to include "the consideration in public sessions of the possibilities of increasing employment; protections against destructive competition and against excessive prices and monopolistic tendencies; the elimination of inequalities and inconsistencies in codes; the position of small enterprises; and the vast problem of code administration and the organization of industry for self-government."

ALTERATION OF LOSS LIMIT CLAUSE.

It is expected that a hearing will be called. At that time the druggists will be permitted to put in all the evidence they have tending to show the inadequacy of a small markup. At the same time it is expected that a compromise proposal which has been worked out in the NRA will be presented for the druggists' consideration.

Just what this compromise proposal will be could not be learned at this writing, but it was expected that it would be made public when formal announcement of the hearing was made. It is understood that the hearing will cover only the loss limitation provision of the retail drug code and will not affect the food code or the general retail code.

MODEL STATE NRA LAW.

Administrator Hugh S. Johnson has made public a "model" State industrial recovery act which has been submitted to governors, together with a diplomatically worded letter pointing out that NRA is "deeply interested" in the passage of measures for coöperation with the Federal law and for elimination of conflicts. Just how far the proposal could be advanced this year is not clear. Relatively few states have regular sessions of legislatures in the even numbered years and while special sessions were set for this year in several, some of these already have been held. Twelve states to date have enacted NRA coöperative legislation: New York, New Jersey, Virginia, Ohio, Texas, California, Utah, Colorado, Wisconsin, Kansas, Massachusetts and Washington.

Though the Administrator's idea looks toward the eventual continuance of codes past the emergency period, the present proposal is purely an emergency plan worded to expire with the Federal industrial act, using as a preamble a declaration of state-wide emergency similar in nature to the Congressional declaration on which the National Industrial Recovery Act is founded.

The immediate problem which calls for state assistance is twofold: A number of Federal judges hearing the relatively few cases so far in court have declared Congress cannot delegate power to regulate business which is not interstate. Machinery for 100 per cent Federal enforcement might prove as cumbersome as prohibition enforcement, in the opinion of NRA officials.

ONLY MEDICINE IS CALLED "GOOD FOR HEALTH" IN TEXAS.

Only medicines and drugs can be labeled as "good for the health," under a new ruling recently made by the Texas Pure Food and Drug Division of the State Health Department. This means that advertising and window displays cannot include the statement that the product is "Good for Your Health," or a similar statement.

In view of this ruling, bakeries in the state which are selling a wheat bread advertised as "Good for Your Health," will be barred from continuing such advertising. It is the opinion of the Pure Food and Drug Division that ingredients of bread and food do not belong in class of health remedies and so cannot bear "health" labels.

MAIL-ORDER HOUSES OPPOSE PRICE-FIXING.

On February 17th, leading mail-order houses placed before General Johnson a comprehensive study of price fixing under codes of fair competition and called upon him to eliminate provisions which compel manufacturers to post for the notice of all competitors current and future prices.

The representatives suggested that collection and dissemination of current price information should be done by NRA administrators

and not by the industry itself through its code authority.

VIRGINIA LEGISLATION.

Liquor Control Act.—H. R. 33, passed the House on February 1st, will allow druggists to sell whisky on prescription, but they must buy liquor supplies from control board stores. Bay Rum must be sold on prescription. It does not control wines and beer of 3.2% or less alcoholic content.

Virginia Trades Practice Act does not define "cost," but an interesting provision makes cut prices unlawful if they tend to substantially lessen competition or unfairly injure a competitor.

Fair Trade Practice Bill makes it unlawful to sell merchandise below cost, and defines "cost" for the retailer as the invoice price or price paid for the goods plus overhead.

VALIDITY OF 20-YEAR-OLD PRICE DISCRIMINATION IN UTAH.

Attorney General Joseph Chez of Utah has brought suit against Safeway Stores, Inc., grocery chain, which will serve as a test of the validity of a twenty-year-old Utah law said never to have been argued in court.

The suit alleges that the grocery firm "did unlawfully and intentionally for the purpose of destroying the competition of an established dealer in similar commodity, to discriminate between different sections within Salt Lake City by selling commodities in one section lower than the price charged for such commodities in another section."

While the case does not involve drug stores, the test is being watched eagerly by druggists because of its application to drug price cutters who use similar tactics.

NEW JERSEY STATE CODE.

Under leadership of the New Jersey State Pharmaceutical Association, pharmacies, drug stores and other types of retailers handling drugs are coöperating to draw up a retail drug code for the state of New Jersey to offer greater protection than does the Federal code.

This action is taken under a law passed by the New Jersey Legislature and approved by the Governor last September, giving the Governor power to set up within the state codes of fair ethics for different lines of business, similar to the power held by the President under the NRA. This law says that the state codes may be approved by the Governor provided they are consistent with the federal codes, but "due regard, however, may be had for local conditions and local customs."

DRUGGIST'S LICENSE SUSPENDED.

License of a New York City pharmacist alleged to have been apprehended imitating a well-known proprietary drug has been suspended by the New York State Board of Pharmacy, George W. Mather, secretary, announces. He states that drastic action was taken in this case because it was found that the pharmacist in question was manufacturing the imitation product himself. Suspension is of indefinite duration, and the board can restore the license or permanently revoke it, as it sees fit.

PHARMACISTS ASK REORGANIZATION OF MISSISSIPPI BOARD.

A bill to reorganize the Mississippi board of pharmacy and strengthen the old law governing the profession of pharmacy in this state has been approved by the House Committee. Under the new bill there is authorized an executive officer, who is secretary of the Board, to be charged with investigating the complaints against pharmacists with authority to employ counsel. The new bill provides for a Board of Pharmacy of four members appointed by the governor from a list of twenty-one submitted by the State Pharmaceutical Association. The executive officer is to be nominated by the association and appointed by the governor.

TREATY SERIES NO. 863—NARCOTIC DRUGS.

Editorial comment was made in the July number of the JOURNAL, page 596, on the ratification of the Narcotics Limitation Convention. The transactions covering this important action is published in pamphlet form and may be obtained from the Superintendent of Documents, Government Printing Office, Washington, D. C., for 50 cents.

We are in receipt of a souvenir booklet of the incorporation of Dartford as a municipal borough on September 13, 1933. Here the Wellcome chemical and galenical works are located. The booklet is finely illustrated and bound, containing views of Dartford and an insignia of the Lord Mayor of London presenting the charter together with the official blazon of the borough of Dartford.

BOOK NOTICES AND REVIEWS.

Handbook of Chemotherapy. By DR. VIKTOR FISCHL, Departmental Director of the Schering-Kahlbaum A.G., Berlin, and PROF. HANS SCHLOSSBERGER, Member of the Reich Board of Health, Berlin-Dahlem. English translation by Dr. A. S. Schwartzman. H. G. Roebuck & Son, Publishers, Baltimore, 1933. 410 pages. Price $8.00.

This English translation of the "Handbook of Chemotherapy" will undoubtedly be considered by all those engaged either directly or indirectly in pharmacological research as one of the most interesting and important recent publications of its kind. The term chemotherapy, as employed by the authors, is the broader and more logical one introduced by a number of modern authors in opposition to the old and restricted word, *chemotherapy*, which Ehrlich applied to the treatment of a few specific blood infections by intravenous injection of certain chemicals, which was expected to result in a *therapia sterilisans magna*. There is no valid reason in modern experimental pharmacology and therapeutics for not applying the term chemotherapy to any and every clear-cut pharmacological effect produced by a definite chemical compound on a specific physiological function; and this is the sense in which the word is employed by Fischl and Schlossberger in their important work, the first volume of which is now available in English. This volume of the "Handbook of Chemotherapy" deals with the so-called "metal-free" organic compounds producing specific pharmacological effects. After a brief introduction, to which are appended references to the general literature on chemotherapy, Chapter 1 begins with the acyclic chlorine compounds. Chloroform, carbon tetrachloride and other chlorinated compounds are discussed in this chapter, and a description is given of their action in relation to their chemical structure. Chapter 2 deals with the unsaturated fatty acids. Here the reader will meet many drugs with which he is familiar and also numerous chemical derivatives from the plant world of which he has probably never heard before. Thus, for instance, in addition to cod liver oil and its derivatives, and the chemistry of chaulmoogra in all its ramifications, he will be confronted by such substances as margosa oil, achaoti oil, nastin, gamelan, and a host of synthetic chemicals related to the various natural products described in this chapter. A third chapter deals with simple benzol and naphthalin derivatives as well as with oxy- and oxo compounds. In this section we have a discussion of the salicylates, the phenols, various anthelmintics and other compounds from the standpoint of chemotherapy and chemopharmacodynamic relationships. Chapter 4 contains a short description of the amino acids, succeeded by twenty-four pages devoted to the chemotherapeutic discussion of all the quinolin derivatives except quinine. In this series are found descriptions of Fourneau 710, plasmochin, various amino quinolins, atophan and many other compounds. Chapter 6 contains a complete discussion of quinin and its derivatives, universally regarded as among the most brilliant achievements of modern chemotherapeutic research. The seventh chapter is devoted to emetin and its derivatives and here, as is the case throughout the book, a résumé is given not only of the pure chemistry but also of the pharmacology, toxicology and therapeutic data concerning the respective compounds. Chapter 8 is devoted to a large variety of plant stuffs, including numerous glucosides and alkaloids, anthelmintics, antimalarial and antidysenteric substances. Chapter 9 discusses the acridin derivatives, while Chapter 10 describes dyestuffs of every conceivable structure except those which contain metals. Here we find a thorough consideration of the nitro and nitroso dyestuffs, such as picric acid and naphthol green; of azo dyestuffs, such as chrysoidin, trypan red, trypan blue and afridol blue; of the carbonium dyestuffs, such as malachite green, auramin, brilliant green, fuchsin, methyl violet, gentian violet and the eosins; of the azin dyestuffs, such as safranin; and of the oxazin and thiazin dyestuffs, including methylene blue. Chapter 11 deals with certain colorless urea derivatives and particularly with the historical germanin, otherwise known as Bayer 205, Fourneau 309, naganol and moranyl; and the final chapter contains a brief discussion from a chemotherapeutic point of view, of blood serum of men and of certain types of apes.

The first volume of the English edition of the "Handbook of Chemotherapy" excels in its physical make-up, the print being remarkably clear and legible, the paper of very fine quality and the binding of durable character. Among the invaluable features of this work are the numerous and exceptionally clear formulas of

all the complicated compounds that must be discussed in any book on chemotherapy. Many excellent tables also add to the value of the book. At the end of each chapter appears an exhaustive bibliography, a conspicuous feature of any such reference work as the volume before us. It is to be hoped that H. G. Roebuck and Son, the American publishers who have made this significant venture, will receive sufficient encouragement from those interested in the advancement of pharmacology and pharmaceutical chemistry to induce them to publish the translation of the other two volumes of the "Handbook of Chemotherapy," a set of which, together with an appropriate index, should have its place among the books of all investigators in this field.—DAVID I. MACHT.

The following reprints have been received from the Wellcome Chemical Research Laboratories:

"The Alkaloids of Picralima Klaineana, Pierre, Part II," by T. A. Henry.

"Apparatus for Continuous Extraction by Chloroform," by H. Paget.

"Echitamine in Alstonia Barks," by J. A. Goodson.

"The Composition of Modern Quinetum," by J. A. Goodson and T. A. Henry.

"Apparatus for Quantitative Catalytic Reduction," by H. Paget and W. Solomon.

"Bases Derived from Some Substituted Propenylbenzenes with a Note on the Preparation of Pure Methylamine," by T. M. Sharp and W. Solomon.

"Experiments on Antimony Compounds Used in the Treatment of Bilharzia Disease and Kala-Azar," by W. H. Gray and J. W. Trevan.

Reprint from *Annales de l'Institut Pasteur* has been published on "The Control of Cordage and Cat Guts." The authors are A. Goris and A. Liot.

AMERICAN CHEMICAL SOCIETY.

The American Chemical Society will hold its 87th meeting in St. Petersburg, Fla., March 25th–30th. Dean Townes R. Leigh, of the College of Arts and Sciences, is the general chairman of the convention; he was formerly dean of the College of Pharmacy, reorganized in 1933 as a School of Pharmacy in the College of Arts and Sciences; B. V. Christensen is the director.

The Florida Medicinal Plant Garden is operated under the supervision of the Department of Pharmacognosy, School of Pharmacy, University of Florida. Dean Leigh was president of the American Association of Colleges of Pharmacy, 1931–1932.

Texas Pharmaceutical Association will probably change its time of meeting, to June 18th–21st; the place remains the same, namely, Mineral Wells, Tex.

The Copeland bill S. 2800 replaces former bills by Senator Copeland. Its purpose is to displace the present Act; hearing on this bill will be held Tuesday, February 27th.

DRUG STORES IN CUBA REOPEN AND PHARMACEUTICAL TRADE BECOMES NORMAL.

On January 24th, retail drug stores in Havana reopened, and the medical strike (which included nurses, hospital attendants, pharmacists, dentists, laboratory workers, undertakers—in fact, all branches of public-health workers and professionals) was brought to a close with the signing of an agreement between the secretary of the Department of Health and the officials of the Medical Federation. This agreement, based on 24 demands, served to stop the strike, which had left the island without health service except for serious emergency cases. All drug stores were closed, but it was stated that the Federation would permit the filling of prescriptions in certain cases which they considered urgent.—Assistant Trade Commissioner Kathleen Molesworth, Havana.

Dr. Wolfgang Schnellbach noted the abstract published in the January JOURNAL on page 30 and refers to an article by him in the *American Journal of Pharmacy* for February 1929, on page 137, entitled "Yeast Extract I Have Known and Satisfactory Applied Mass Excipient." The abstract published in the January number is from the *Weekblad*, reference to which is given.

We are glad to call attention to the article by Dr. Schnellbach.